BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

UNIVERSITY OF MICHIGAN
JAN 1 1956
MEDICAL LIBRARY

SATURDAY DECEMBER 31 1955

TABLE OF CONTENTS

Acute Infections of the Chest in General Practice A. Batty Shaw, D.M., M.R.C.P., and John Fry, M.D., F.R.C.S. 1577

Argentaffin Carcinoma of Ileum with Raised Serum 5-Hydroxytryptamine David Duncan, M.B., F.R.C.S.Ed., Jean D. Garven, Ph.D., B.Sc., and James L. Gibbons, M.B., M.R.C.P., D.P.M. 1586

Serial Biopsy in Ulcerative Colitis S. C. Truelove, M.D., M.R.C.P., A. R. Horler, M.D., M.R.C.P., and W. C. D. Richards, M.B. 1590

Giant-cell Arteritis with Aneurysms R. J. Harrison, M.R.C.P., C. V. Harrison, M.D., and H. Kopelman, M.D., M.R.C.P. 1593

Giant-cell Arteritis of the Legs R. Finlayson, M.B., and J. O. Robinson, M.Chir., F.R.C.S. 1595

Nasal Granuloma and Periarteritis Nodosa Paul F. Milner, M.B. 1597

Malignant Change in Erythema ab igne G. A. Grant Peterkin, M.B., F.R.C.P.Ed. 1599

Pneumatosis Cystoides Intestinalis J. D. Griffiths, M.B., F.R.C.S., and D. F. Ellison Nash, F.R.C.S. 1602

MEDICAL MEMORANDUM

Papaverine in Traumatic Arterial Spasm after Supracondylar Fracture of Humerus. P. Abbey, F.R.C.S. 1604

BOOK REVIEWS 1605

REFRESHER COURSE

Coronary Thrombosis. A. Morgan Jones, M.B., M.Sc., F.R.C.P. 1613

GENERAL ARTICLES AND NEWS

The Heberden Society 1616
Preparations and Appliances 1617
New Minister of Health 1617
Medical Notes in Parliament 1626
Vital Statistics 1628
Medical News 1630
Births, Marriages, and Deaths 1631
Questions and Comments 1632

OBITUARY

C. F. Fernando, C.M.G., O.B.E., M.D., M.R.C.P. 1624
C. H. Allen, O.B.E., M.B., F.R.C.S.Ed. 1624
D. J. Browne, M.B. 1624
Samuel Hall, M.B. 1625
H. G. Downer, M.B., D.L.O. 1625
D. G. Williams, M.R.C.S. 1625

LEADING ARTICLES

Hepatic Insufficiency 1607
Employment of the Elderly 1608
Carcinoma in Situ 1609

ANNOTATIONS

Initiation of Visual Sensation 1610
Pulmonary Hyaline Membrane 1611
Conception During Lactation 1612
Mental Illness and the Law 1612

CORRESPONDENCE

Toxic Goitre. A. G. Macgregor, M.D., and E. J. Wayne, M.D.; C. Lenore Simpson, D.M. 1618
Carotid Sinus Syndrome. E. Rogans, M.B. 1618
Syphilis. G. H. Knight, M.D., and W. Fowler, M.D. 1618

SUPPLEMENT

Full Contents on First Page of Supplement

General Medical Services Committee 183
Rating and Valuation 184
Scottish News 185
Correspondence:
Legal Detention and National Insurance. J. F. MacMahon, M.D. 185
Doctors and the Press. F. Ray Bettley, M.D. 186
Entry into General Practice. G. R. C. D. Gibson, M.B. 186

CORRESPONDENCE—*contd.*

Forty Years On. S. Brook, D.I.C.; T. David Lambert, M.B. 1618
Centipede Bites. E. R. Blay, M.B. 1619
Rib Fractures. Z. Rix, M.D. 1619
Dimenhydrinate. G. S. Mansell, M.R.C.S. 1619
Thiopentone. J. R. Cross, M.B., D.A. 1620
Chlorpromazine. J. A. Beal, M.R.C.S. 1620
Isoniazid. G. Chasapakis, M.B. 1620
Extradural Haemorrhage. N. Whalley, F.R.C.S.Ed. 1620
Porphyria. E. Saphier, M.R.C.S. 1620
Sore Throat. I. H. J. Bourne, M.B. 1621
Nicotine Dosage. L. M. Johnston, M.B. 1621
Antenatal Pulmonary Embolism. C. G. Warnock, M.D. 1621
Heroin. N. A. Sprott, F.R.C.S.; G. F. Fielding, M.D.; R. C. McLaren, M.B. 1621
Physiotherapy. J. H. Cyriax, M.D. 1622
Post-herpetic Neuralgia. Joyce Massey, M.C.S.P. 1622
Post-partum Haemorrhage. H. E. Reiss, B.M. 1622
"Modern Health Series." Lord Horder 1622
Homosexuality and Prostitution. S. L. Sherwood, L.R.C.P.Ed. 1623
Chronic Perionychia. G. B. Mitchell-Heggs, M.D., and M. Feiwel, M.B. 1623
Flavoured and Sweetened. G. H. Alabaster, M.D. 1623
Restoration of Breathing after Presumable Death. M. D. Ripka, M.R.C.S. 1623

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON, W.C.1

No. 4986, WEEKLY, PRICE 3/-

Copyright

REGISTERED AS A NEWSPAPER

first line of defence . . .

. . . against the rigours of winter

In a very real sense, the body's first line of defence is furnished by the cilia of the nose. Any damage to the mucosal cells may interfere with ciliary action and so open the way to infection. How important it is, during these months of "peak infection" risks, to choose with care the nasal drops so many patients need. Research has shown conclusively that ARGOTONE contains no substances which can harm the nasal mucosa. Presenting silver vitellin in company with ephedrine hydrochloride, ARGOTONE is quick to reduce the swollen mucous membranes and to restore permeability to the nasal sinuses—yet there is no risk that ciliary action will be inhibited.

ARGOTONE is available in a convenient plastic atominer. Ensures swift penetration of ARGOTONE throughout the naso-pharynx.

ARGOTONE "READY SPRAY"
Basic N.H.S. price 2s. 10d. containing approx. 15 c.c. Argotone. Available on Form E.C.10.

ARGOTONE
NASAL DROPS

Basic N.H.S. price 2s. 6½d. per bottle of 20 c.c. May be prescribed on Form E.C.10. Available in the British Commonwealth, Colonies and 15 other countries. Sample on request.

℞

RONA LABORATORIES · 12-13 MOLYNEUX STREET · LONDON W.1. · Ambassador 4437/8.

Oxygenaire

RENTALS, SALES AND MAINTENANCE SERVICE

PHONE

LONDON: WELbeck 4477 (10 lines)

BELFAST: Belfast 69266
BIRMINGHAM: Victoria 2484
BRISTOL: Abson 281
CARDIFF: Cardiff 31361
EXETER: Topsham 3070
GLASGOW: Bearsden 4373
LEEDS: Leeds 59111
MANCHESTER: Sale 5620

for DAY and NIGHT service or write to 8 Duke Street, London, W.1., for particulars of Maintenance Service and Sales.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 31 1955

ACUTE INFECTIONS OF THE CHEST IN GENERAL PRACTICE

BY

A. BATTY SHAW, D.M., M.R.C.P.
Senior Medical Registrar, Guy's Hospital

AND

JOHN FRY, M.D., F.R.C.S.
General Practitioner

Disorders of the respiratory tract account for the largest group of organic conditions encountered in general practice to-day. In analyses of general practice, they have been shown to account for 33% of the attendances in eight Yorkshire practices (Pemberton, 1949), 24% in ten practices from different parts of the country (Logan, 1953), and in south-east England figures of 20% from a rural practice (Taylor, 1954) and 25% from a suburban practice (Fry, 1955) have been reported. Infections of the upper respiratory tract account for 60% and, of the lower respiratory disorders, acute infections account for more than half the attendances.

Many studies of acute chest infections have been made in hospitals and among Service communities, but in this country they have seldom been undertaken in general practice. It was therefore decided to make such a study, with the aid of the full diagnostic facilities that are normally only practicable in hospital, during the winter of 1954–5. This was achieved by a co-operative study between a group of practitioners and their local hospitals, one of us (A. B. S.) acting as intermediary for the collection of specimens and the clinical co-ordination of the work.

The main aims of the investigation were fourfold: (1) a clinical study of acute infections of the lower respiratory tract in general practice; (2) a detailed investigation of these infections; (3) to make observations on treatment though no controlled therapeutic trial was attempted; and (4) to correlate the clinical and investigative data, noting which of the latter were of most practical value under the conditions of general practice.

Materials and Methods

Patients.—The cases of acute infective chest disease occurred in the practices of eight practitioners* in south-east London between October 1, 1954, and May 1, 1955 (see Fig. 1). A total of 80 cases were studied (44 males and 36 females). The ages of the adult males ranged from 16 to 76 (average 44.9 years) and of the adult females from 16 to 88 (average 38.3 years). Children under the age of 16 were excluded, though an exception was made with five children who formed part of family outbreaks of influenza. The object of the tests was explained to each patient, emphasizing that, in addition to this being an investigation of a general problem, the results would be of immediate value in their personal management.

Area and Weather.—The patients were derived from a residential suburban district in the south-east outskirts of London. They were from social classes IV and III, with some from class II. They were principally employed in local light industries and in clerical and administrative duties in central London. In October and November, 1954, there was a dry period of weather, which was followed by a cold spell, with snow in January, 1955. Slight fog was present for three days in February. It was an "average winter" so far as illness in general practice was concerned.

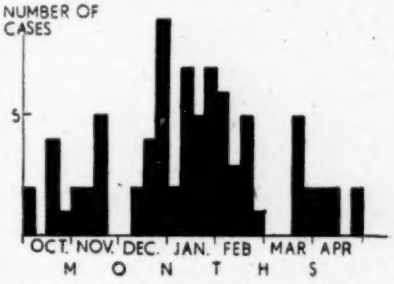


FIG. 1.—Time of onset of 80 cases of acute chest infection, October, 1954, to May, 1955.

Clinical Criteria of Cases for Study.—The patients studied were those with clinical features of an acute infection of the lower respiratory tract, severe enough to confine them to bed at home. We excluded mild relapses of chronic bronchitis, as the numbers of these which would have occurred would have been too great for our facilities to investigate, but severe infective relapses were included. The cases we set out to investigate were those which are included by such diagnostic labels as acute pleurisy, bronchopneumonia, influenza with chest complications, lobar pneumonia, and others.

Method of Study.—Each practitioner participating in the scheme was responsible for the clinical care of his patients throughout the investigation and managed them in his normal way, but keeping details of the clinical data on a form. When first called to a case of acute infective chest disease, he informed one of us (A. B. S.), who visited the patient in his home within the next twenty-four hours, repeated the clinical examination, and took specimens for examination to a local hospital

*Drs. C. H. Comrie, D. I. Finer, J. Fry, J. G. Goodhart, W. S. Hunt, V. J. Marmery, T. W. Renton, and M. K. Thompson.

laboratory. If practicable, the initiation of specific treatment was delayed until the specimens had been taken, but this could not always be achieved. Each patient was visited a second time by A. B. S. during the third week of illness for the collection of a second sample of blood. We were anxious to investigate patients early in the course of their disease, and that this was achieved is shown by Fig. 2. It will be seen that 72 out of the 79 patients (91%) were first seen for the collection of bacteriological and other specimens within five days of the onset of symptoms.

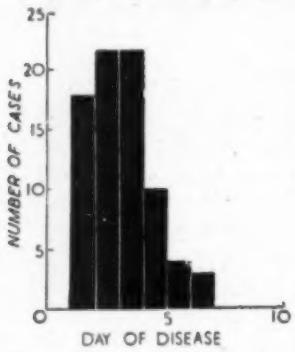


FIG. 2.—Day of disease when bacteriological and other samples were collected from 79 cases of acute chest infection. The eightieth case was seen in the first week of clinical illness, but initial specimens were not taken until the fourteenth day (Table V, Case 62).

INVESTIGATIONS

The investigations included a full examination of the blood taken at the first visit (haemoglobin, white blood cell count, and erythrocyte sedimentation rate) and estimation of cold agglutinins in the first and second samples.

Throat swabs and pernasal swabs were taken at the time of the first visit, and if the temperature was above 100° F. (37.8° C.) blood was taken for culture. Sputum was collected for examination if available and, if not, a wax carton was left with the patient for later use and delivery to the local hospital laboratory by a friend or relative.

Gargles for virus study were collected in a vacuum flask of ice if the patient was seen within five days of the onset of illness. Paired specimens of blood were examined for serological evidence of infection by influenza, Q fever, the psittacosis/lymphogranuloma venereum group of viruses, and against the streptococcus M.G.

Chest radiographs were arranged by the practitioner of each case. If he thought that there was clinical justification arrangements were made for a domiciliary chest radiograph during the acute stage of illness: if not, the patients were radiographed as soon as they were fit to attend a local hospital. Lateral radiographs were taken in cases when abnormality was shown on the postero-anterior chest film, but for practical reasons they were not performed in every case. Abnormal pulmonary changes were followed up by serial radiography.

Clinical Classification

The most satisfactory classification of disease is on an aetiological basis, but the acute infections of the lower respiratory tract are difficult to differentiate in this way in general practice and are the subject of much terminological confusion.

Among the reasons for difficulty in their differentiation are: (1) the special features of the pathology of acute infections of the lower respiratory tract, which has only a limited response to attacks by pathogenic bacteria and viruses: the same clinical picture may be produced by different infective agents, and, conversely, the same infection may cause varying clinical syndromes; (2) even when full investigations are carried out, the aetiology cannot always be determined with the tests at present available; and (3) the tests which are available for their investigation are either difficult or time-consuming to carry out in general practice and there may even be no local facilities to have them undertaken.

As a result of such difficulties, the practitioner has to adopt a practical classification of his cases, based primarily on a clinical assessment of the patient, in which descriptive rather than aetiological terms form the basis. There is no generally agreed classification of these cases, but we divided them by their mode of clinical presentation into three main groups: (1) influenza with chest complications, (2) bronchitis, and (3) pneumonia. Table I shows the number of patients in the three clinical groups and their age and sex distribution.

TABLE I.—*Age and Sex Distribution of the Cases of Influenza with Chest Complications, Bronchitis, and Pneumonia*

Group	Sex	Age in Years								Total
		10–	20–	30–	40–	50–	60–	70–	80+	
1	M	4	1	3	1	1	—	—	—	10 } 27·5%
	F	4	4	—	2	1	1	—	—	12 }
2	M	1	1	1	2	1	6	1	—	13 } 20%
	F	—	—	1	1	—	—	—	1	3 }
3	M	2	2	3	5	3	3	2	—	20 } 52·5%
	F	2	5	3	5	3	2	2	—	22 }
Total		13	13	11	16	9	12	5	1	80

Group 1. Influenza with Chest Complications (22 Cases, 27.5%)

The diagnosis of influenza is often inaccurate when applied to the true sporadic case, but this is not so during times of epidemic. During the investigation there was a proved outbreak of influenza B in the area and there was therefore justification for diagnosing influenza in those with its clinical features, but only cases whose respiratory-tract symptoms were a prominent feature of their illness were included.

Of the 22 cases, none had clinical consolidation, eight had a local area of moist sounds, and in nine there were widespread and bilateral rhonchi and rales. In five cases no abnormal signs were elicited.

The clinical course of these cases showed nothing worthy of remark—none was severely ill and all recovered rapidly without any serious complications.

Group 2. Bronchitis (16 Cases, 20%)

Bronchitis was diagnosed in those cases in which the infection appeared to be predominantly bronchial; their differentiation from "pneumonia" was at times extremely difficult and was made from two main clinical criteria: First, in those cases with diffuse rhonchi and rales over both lung fields, the cases of "bronchitis" were distinguished from the "pneumonias" only by the degree of clinical severity of the illness; second, any case with predominantly localized signs, irrespective of the degree of illness, was classified as "pneumonia." As a consequence of adopting these definitions for the diagnosis of "bronchitis," none of the patients in this group was severely ill, the temperature was never above 100° F. (37.8° C.) in any case, and all exhibited signs of scattered diffuse and bilateral rales and rhonchi in varying degrees. Cases were divided into two subgroups: those with acute bronchitis and no previous pulmonary disease, and those with acute relapse and who were subject to chronic bronchitis. Seven patients were included in the first and nine in the second subgroup. In six of the seven cases included in the former subgroup bronchitis was preceded by an infection of the upper respiratory tract and in only one of the latter.

Group 3. Pneumonia (42 Cases, 52.5%)

The classification of pneumonia has undergone radical alteration in recent years, but many different systems are still used by the authors of standard textbooks of medicine. We are in full agreement with the current trend that pneumonia is best classified on an aetiological basis, but it is often difficult or even impossible to find an aetiological label for many of these cases, even with full ancillary investigations in hospital, and the difficulties are even greater in general practice, where fewer facilities for investigation are available.

Of the many classifications of pneumonia, that proposed by Scadding (1952) is the most acceptable, and in this paper we applied his classification to cases of "pneumonia" when encountered in the home, and observed the correlation that was obtained when the cases were fully investigated. Scadding has classified pneumonia into three main groups—bacterial, viral, and aspiration. The first two groups are self-explanatory; the aspiration pneumonias he defines as "those due to failure of the normal defences of the respiratory tract, allowing organisms not specifically pathogenic to gain access to the pulmonary acini . . . their later course being influenced by the bacterial flora." Among those included in this group are patients whose pneumonia follows acute or chronic catarrh of the upper respiratory tract, and those who are the subjects of long-standing pulmonary disease, such as chronic bronchitis. These two groups can readily be recognized by the practitioner, and we found that 29 of our 42 cases of "pneumonia" fell within this definition.

The remaining 13 cases were provisionally classified as bacterial pneumonia; for the diagnosis of virus pneumonia, Scadding's third group, is seldom made by a practitioner when he first encounters a case, unless in the presence of a known epidemic (Table II).

It is of greater immediate concern to a practitioner to know whether pneumonia is present than its exact aetiology, and, although much has been written on the treatment of pneumonia in general practice, little work has been done on methods of diagnosis. In general practice pneumonia usually presents as an illness of fairly sudden onset, and the diagnosis has to be made in the first place on clinical grounds. In the next section we discuss the great help which a practitioner may derive from radiography in a suspected case, but this is not always necessary nor is it always available. In this section the clinical diagnosis is discussed.

TABLE II.—*Clinical Distribution of 42 Patients with "Pneumonia"*

Previous History. Physical Signs	Possible Aetiology			Total
	Bacterial Pneumonia	Aspiration Pneumonia		
	No Previous History of Chronic Lung Disease or U.R.I.	Preceding U.R.I.	Chronic Bronchitis	
Consolidation	2	1	1	4
Local rales	9	8	2	19
Diffuse rales and rhonchi	2	2	9	13
Pleural rub		2		2
No abnormality ..		4		4
Total ..	13	17	12	42

The clinical criteria on which the diagnosis of "pneumonia" was made in 42 cases were the severity of the respiratory illness and the presence of local signs of pulmonary inflammation. By adopting the first criteria many patients with generalized rales and rhonchi were diagnosed as "pneumonia" who might have been classified by others as cases of "severe bronchitis," but the diagnosis of "pneumonia" was made because of the severity of their constitutional disturbance. The second group included those who had varying degrees of clinical illness other than suspected influenza. It is in the clinical diagnosis of suspected pneumonia that the practitioner may have to place greater reliance on physical signs than his hospital colleagues, to whom radiology is so more readily available. The cases have therefore been divided into five groups on the basis of the abnormal physical signs which were elicited when the patients were first seen or within the first few days of illness.

The results are shown in Table II. It will be seen that an area of localized rales (one of the criteria for the diagnosis of "pneumonia") and diffuse rales and rhonchi were the two sets of signs most often encountered. Signs of consolidation were detected in only four cases suspected of having "pneumonia" (9.5%).

The cases of "pneumonia" included the most severely ill patients in the series, and the only four cases, out of the total of 80, who required admission to hospital all presented in this way. One was admitted because he was too ill to be nursed at home, two because of inadequate home facilities, and one because of failure to respond to specific therapy at home.

Radiography

Seventy-three patients were radiographed during the course of their illness, five refused a radiograph, and in two the investigation was overlooked.

Relevant pulmonary abnormalities were detected in 35 of the 73 cases (48%). The earlier the radiograph was taken the higher was the percentage of abnormalities revealed. Table III shows the number of cases radiographed

TABLE III.—*Week of Illness in which the First Radiograph was Taken (73 Cases) and the Number and Percentage with Abnormalities*

Week:	1	2	3	4	Total
No. of cases	32	21	17	3	73
No. with radiological abnormalities	25	7	2	1	35
Abnormalities	78%	24%			

in the different weeks of illness and the percentage of abnormalities. In the 32 patients who were radiographed in the first week, 25 had pulmonary abnormalities (78%); 22 of these were radiographed on a domiciliary visit, of which 18 showed abnormalities (82%). Only 10 out of the 41 who were radiographed after the first week at local hospitals showed significant pulmonary changes (24%).

These two sets of cases are not comparable, because the group who were radiographed early in their illness contained more patients who were severely ill and who would normally have a chest radiograph, and the second group included the milder cases which might not have had a radiograph had they not been included in the investigation.

The abnormalities detected in the 35 patients included one with unsuspected evidence of bronchial obstruction which was later proved to be due to a bronchial carcinoma, and one who developed a spontaneous pneumothorax. The remaining 33 radiographs showed evidence of pneumonic change. These have been divided on an anatomical basis into lobar, lobular, and segmental changes, after Crofton *et al.* (1951). Lobar pneumonia denotes a pneumonic process involving the whole of one lobe. Cases in which there is a patchy opacity in the radiograph, which might be in one or both lungs, were called lobular pneumonias. Segmental pneumonias were those in which there was a uniform rather than mottled shadowing, but which occupied less than a complete lobe, and in most of these the segmental distribution was confirmed by a lateral film. Segmental pneumonias (19 cases) formed the largest group, of which three were bacterial in origin and 16 were aspiration pneumonias.

There were 10 lobular pneumonias. Four were due to virus infection, three to bacteria, and three were aspiration pneumonias. Lobar pneumonia was diagnosed in only four cases, of which three were bacterial and the fourth was an aspiration pneumonia of the middle lobe.

Radiography was the most helpful of the investigations that were undertaken. It enabled a correlation to be made with the clinical findings, and it also served to exclude other types of disease such as tuberculosis, of which we found no case, and bronchial neoplasm, of which there was one. The earlier that the radiograph was taken the higher was the proportion of abnormalities, but of greater importance were the films taken after clinical recovery to ensure that resolution was complete.

Bacteriology

In the hospital investigation of cases of acute infective chest disease, negative bacteriological results are frequently attributed to previous domiciliary treatment with antibacterial agents; the present investigation gave an opportunity to study the bacteriology early in the course of illness. In 62 patients specimens were obtained before the start of antibacterial treatment and in 18 therapy had been started within the previous twenty-four hours.

In spite of this early collection of specimens, pathogenic bacteria were isolated from only 25 of the 80 cases (31%). The number of positive isolations from the different sources is shown in Table IV. It will be seen that the highest percentage of positive isolations was from the sputum (25%), followed by throat swabs (18%), and pernasal swabs (11%). No isolations were made from 18 blood cultures taken when there was a fever of over 100° F. (37.8° C.).

TABLE IV.—*Results of Positive Bacteriological Tests*

Source	Bacteria						No. of Positive Tests*	Total No. Tests	Positive Tests
	Str. pneumoniae	*Staph. aureus*	*Str. pyogenes*	*E. coli*	*B. proteus*	*H. influenzae*			
Throat swab	6	2	—	1	1	4	13	72	18%
Nasal swab	2	4	—	1	1	2	8	71	11%
Sputum	5	2	1	—	—	5	13	51	25%
Blood culture	—	—	—	—	—	—	—	18	—
Total	13	8	1	2	2	11	34	212	16%

* Where more than one organism was isolated from the same specimen it is shown as one positive result in this column. Further details in other columns.

The organisms most frequently isolated were *Streptococcus pneumoniae* (13), *Haemophilus influenzae* (11), and *Staphylococcus aureus* (coagulase-positive) (8). In 26 instances the sputum was cultured on Löwenstein's medium but no tubercle bacilli were grown. Sensitivity tests to antibiotics were not performed as a routine.

The isolation of a pathogenic organism, especially from a throat or pernasal swab, was not necessarily regarded as the cause of the concurrent respiratory illness. In analysing the bacteriological results we considered them in relation to the clinical, radiological, and other pathological findings, to the source of their isolation, and to the profuseness of their growth. In 14 of the 25 patients (17.5% of the total, 80) from whom pathogenic organisms were isolated, they were regarded as the cause of the infection, and in 11 their presence was not thought to be of primary aetiological significance.

The low percentage of positive bacteriological isolations, even from sputum, was disappointing. Seventeen patients claimed to have no sputum, and 12, who reported sputum at some stage, failed to send specimens for examination; therefore sputum was examined from only 51 of the patients and only one specimen was examined from each case. Of the sputum specimens received by the laboratory, some consisted of saliva, and the desiccated state of a few indicated the time they had been in transit; it was not surprising that these often gave negative results, and it was concluded that the only method of ensuring that the laboratory received a fresh and adequate specimen was for a practitioner to collect and deliver the sputum personally. It was not our intention to adopt special bacteriological techniques, but merely to have the specimens examined in the standard way that was used by the local hospitals. The results would undoubtedly have been different if we had employed special techniques, but there is no point in commenting on these unless proper specimens are first received by the laboratory. But, using simple and commonly accepted techniques, and with better facilities for collection than normally attain in practice, we had a small reward for a considerable amount of labour in collecting and culturing the specimens.

Virus Studies

Investigations for evidence of virus infection gave positive results in 15 of the 80 cases (18.8%). Two tests were used: an attempted isolation of viruses from throat garglings and the examination of paired sera for a change in the antibody titre.

Garglings were collected from 67 cases seen within five days of the onset of the illness, but in no instance was a virus grown.

Paired sera were examined from 70 cases, of which 50 gave negative results. In six the results were equivocal and in 14 the titres were considered to be diagnostic of recent virus infection—that is, they showed either a fourfold rise in titre or a high titre which subsequently fell. Of the positive cases, eight showed evidence of influenza B, one of influenza A, and two of psittacosis; three showed titres against streptococcus MG which are acceptable for the diagnosis of virus pneumonia, and these also showed a significant elevation of cold agglutinins. A fourth case, with a negative streptococcus MG titre, was also diagnosed as a virus pneumonia on the basis of a fourfold rise in cold agglutinins, leucopenia, and the clinical features (Table V).

TABLE V.—*Investigations in Four Cases of Virus Pneumonia and Two Cases of Psittacosis*

Case No.	Day of Disease*	Complement-fixation Tests		Cold Agglutinins	W.B.C.	Radiograph
		Psitt. L.G.V.	Aggl. Strep. MG			
			Virus Pneumonia			
12	7/14 24/31	0 0	1/80 1/10	1/128 1/64	6,000	Lobular shadows right upper and lower lobes
24	4 16	N.T. 1/8	N.T. 1/10	1/8 1/32	3,000	Lobular shadow left upper lobe
34	3/11 17/25	0 0	1/10 1/80	1/1000 1/128	9,000	Diffuse lobular opacities in right lung
40	3 16	0 0	1/40 1/160	0 1/128	6,000	N.A.D.
			Psittacosis			
61	5 16 32	— 1/256 1/128	— 0 0	0 1/16 —	10,000	N.A.D.
62	14 30	1/1024 1/512	0 0	— —	12,000	Lobular shadow right lower lobe

* Days of preliminary and main clinical illness; sera taken on days shown to right of oblique line.

Our results in testing for virus infection were shown to be of limited practical value. We met with no success in isolating viruses from garglings in spite of the great care that was taken in collecting and transporting the specimens. The serological tests had two practical limitations: (1) there was an inevitable delay of at least four weeks from the onset of illness before the results were known, and (2) they required two venepunctures—a procedure unwelcome both to a busy practitioner and to the patient, who has usually recovered by the time the second specimen has to be taken, although in urgent cases a result could be obtained in 10-20 days. But the positive results in 18.8% of cases were of great clinical interest, especially in confirming the diagnosis of influenza and revealing two unsuspected cases of psittacosis.

Haematology

The white-cell counts excluded such general conditions as glandular fever, and of a total of 75 counts 54 (72%) were within the normal range. Three, with virus infections, showed a leucopenia of below 4,000 per c.mm., and 18 had a leucocytosis above 15,000 per c.mm., the highest figure being 42,000 per c.mm. in a case of pneumococcal pneumonia.

The E.S.R. was carried out in 66 cases; it was normal in 11 and raised in 55, the highest figure being 113 mm. per hour in a virus pneumonia.

No cases of anaemia were discovered by performing a routine haemoglobin estimation, for which the levels ranged from 76% (11.2 g.) to 108% (16 g.), with an average of 88% (13 g.).

Cold agglutinin estimations were carried out in 63 cases. Four cases showed a significant rise in titre, all of which had other evidence of virus pneumonia.

The full investigation of acute pulmonary infection includes an examination of the blood, but the results obtained in this survey were of no great practical value to the practitioners. Leucopenia favours a virus infection, and a leucocytosis is against such a diagnosis, but in most of our cases, including three of virus pneumonia and nine of influenza, the count was within normal limits and did not help in establishing the diagnosis. The E.S.R. is a simple ancillary test in assessing a pneumonia that is slow in clearing, and, if raised, may lead to recognition of previously unsuspected carcinoma or tuberculosis. Apart from this, it was not found of great value, and we believe that all cases in which the practitioner is suspicious enough of tuberculosis or carcinoma to investigate the serial sedimentation rates are better referred to the appropriate consultant at the first opportunity.

Correlation of the Clinical Findings and Investigations

One of the aims of our investigation was to determine the aetiology of a representative series of acute infections of the chest in general practice. As a result of our studies we were able to prove a specific bacterial or viral aetiology only in 26 of the 80 cases (32.5%). The limitations of our methods of investigation and of the tests themselves have been referred to, but from the results obtained it had to be concluded that most of our cases (67.5%) were non-specific respiratory infections with an at present unknown aetiology. This being the case, it was apparent that our investigations would be of limited help in giving guidance in attempting an aetiological diagnosis of acute respiratory disease. On the other hand, our largely negative results have revealed the limitations of our methods of investigation and our knowledge of aetiological agents. The 26 cases of proved aetiology consisted of 11 cases of bacterial aetiology and 15 cases of viral aetiology (influenza, 9; psittacosis, 2; "virus" pneumonia, 4). (There was also one bronchial carcinoma.)

Influenza (22 Cases)

The clinical diagnosis of influenza was confirmed serologically in seven cases and there was good reason for believing that the diagnosis was correct in at least four other cases. These four cases occurred in two family outbreaks of influenza, in which all members were ill, either concurrently or simultaneously, and in each of which there was one member whose influenza was proved serologically.

Although the serological test for influenza gives a positive result in a greater proportion of cases than isolation of the virus from gargling, it is not necessarily positive in all cases. In institutional outbreaks, when a large number of persons are infected with influenza, a varying percentage will have negative titres, and instances are on record where the virus has been isolated from garglings but the serology remains negative (Stuart-Harris, 1953). As well as the four clinical but non-proved cases referred to, there were others in which the circumstantial evidence was not so strong, but which also may have been true influenza.

As influenza symptoms may be mimicked so closely by other infections of the respiratory tract it was expected that more diverse diagnoses would be revealed by investigation than was in fact the case. Two patients in the group had evidence of virus pneumonia, though one settled within a few days with only the non-specific therapy for influenza, and two were non-specific respiratory aspiration pneumonias. In 12 cases, including the four of clinical but not proved influenza, all investigations were negative.

Though only a third of the suspected cases of influenza were proved, the correlation between the clinical and investigative findings was satisfactory. However, the results reaffirmed our belief that the diagnosis of influenza should be limited to times of known epidemic, when it can then be made with a reasonable chance of being correct.

"Bronchitis" (16 Cases)

The cases of "bronchitis," which formed the smallest of the three groups, were divided into those without preexisting pulmonary disease and those with a history of chronic bronchitis or other chronic pulmonary disease.

Of the seven cases diagnosed as bronchitis without previous pulmonary disease, all investigations were negative in four; the remaining three had a previous history of nasal catarrh and two were of non-specific aspiration pneumonia. The third, a man with upper respiratory catarrh, mild general malaise, and a presumed area of aspiration pneumonia in his right lower lobe, had a titre against psittacosis which rose to 1/1024 (see Table V). This man's illness was so mild that he was never given specific therapy, and he recovered spontaneously within two weeks, before the results of serological tests were known.

Of the nine patients with a past history of chest disease, eight had chronic bronchitis and one bronchial asthma. All had a normal radiograph, pathogenic bacteria were recovered from the sputum of four, and all virus tests were negative except in one patient, diagnosed originally as a case of infective relapse of bronchial asthma, who later had evidence of psittacosis. This patient was the wife of the other case of psittacosis, but although her illness ran a more severe course than that of her husband, she was at no time more than moderately ill and her chest radiograph was normal.

The diagnosis of "bronchitis," like "influenza," may be made erroneously when almost any pulmonary disease may be the cause, and it was not surprising that three patients had an area of aspiration pneumonia, in particular as the illness in all three was preceded by upper respiratory catarrh. The only result of note was the detection of two cases of previously unsuspected psittacosis. Neither of them had had anything but minor respiratory illnesses, and both had recovered by the time the results of serum tests were known. Their infections occurred during a spell of very dry weather, and, in the absence of any other obvious source, was thought to have been contracted from the birds they fed in large numbers in their garden. Their illnesses were of interest for two reasons: (1) as a reminder of how mild the course of psittacosis may be (Bedson, 1955), and (2) to demonstrate how unusual diseases may go undetected in the guise of non-specific infections of the respiratory tract.

"Pneumonia" (42 Cases)

The results of the investigations in the 42 cases of "pneumonia" are considered in relation to the clinical diagnosis of "bacterial or aspiration pneumonia" and to the presenting physical signs.

Relation of Investigations to Possible Clinical Diagnosis of the Aetiology

A practical difficulty of applying Scadding's classification of pneumonia is that two of his groups are aetiological—namely, bacterial and virus—and the third, aspiration pneumonia, is a descriptive designation. There is therefore no reason why a given case of pneumonia may not logically belong to one of the first two groups and also to the third. Thus specific bacteria may be isolated from a case of aspiration pneumonia, and we have decided, after obtaining Dr. Scadding's advice, that such cases are properly transferred to the bacterial group in discussing the cases on an aetiological basis.

Of the 29 cases diagnosed as aspiration pneumonia, a specific bacterial aetiology was established in three, and one had evidence of virus pneumonia. A fifth case demonstrated the complexity of classification and clinical presentation.

A man presented with "pneumonia" and a history of a cough for five months. His radiograph showed an opacity in the right upper lobe, he had lost weight, and the clinical picture was suggestive of bronchial carcinoma. Arrangements were therefore made for him to be seen at Brompton Hospital for an opinion regarding bronchoscopy. In the five days that elapsed before his appointment his chest had cleared radiologically and he returned home. Pathogenic bacteria had been isolated from his throat swab, and he was therefore regarded as a case of uncomplicated aspiration pneumonia from a chronic sinus infection, which had now been detected. The results of virus studies were then received, which showed that at the time of his acute illness he had been suffering from influenza A.

A sixth case, presenting as an aspiration pneumonia in a man with chronic bronchitis, failed to respond to treatment, and the breath sounds over the right lung became diminished. Radiography revealed changes suggestive of a bronchial obstruction, which later proved to be due to a carcinoma.

Of the remaining 23 cases, where bacterial and virus tests were negative, the chest radiograph showed an area of pneumonia, usually segmental, in 14, and the final diagnosis was aspiration pneumonia. The radiograph was normal in nine, most of which were "pneumonic" exacerbations of chronic bronchitis. They were not all radiographed early in the course of illness, but even had their early radiographs been normal the diagnosis of pneumonia appeared justified on clinical grounds. All were acutely ill, with an average fever of above 103° F. (39.4° C.), marked constitutional disturbance, and purulent sputum. In these severe infective relapses of bronchitis it is reasonable to believe that the bronchial inflammation had spread to peribronchial alveoli. This view is supported by the careful morbid anatomical study of chronic bronchitis by Reid (1954), who demonstrated abscesses in small bronchioles and pneumonic changes in alveoli, which not only might have been too small for radiological demonstration, but could readily have been missed in routine inspection of the specimens.

Of the 13 cases diagnosed as "bacterial pneumonia" in the absence of past or present respiratory catarrh, four had normal radiographs and negative virus and bacteriological tests. Of the nine with abnormal radiographs, six were pneumonias of bacterial origin, and one was a virus pneumonia. In two, all the ancillary investigations were negative, and, while they may have been mild virus pneumonias, they were classified as aspiration pneumonias.

Thus of the 42 cases of clinically suspected "pneumonia," the diagnosis was confirmed in 29 (69%), and reasons have been given for believing that the diagnosis was justifiable in a number of the 13 cases where the radiograph was normal. It was to be expected that the number of abnormal radiographs would be largest in this group, and it was inevitable that not all the suspected cases of pneumonia would have the diagnosis confirmed radiologically.

Relation of the Investigations to the Presenting Clinical Signs

When the abnormal physical signs were correlated with the results of the investigations, the main finding was that the more definite the signs of "pneumonia" the greater was the percentage of abnormal radiological and pathological investigations.

The diagnosis was confirmed radiologically in all four cases with signs of pulmonary *consolidation*. One was a bacterial pneumonia, one an aspiration pneumonia, and the other two were virus pneumonias. It is of interest to note that two of the four cases were virus pneumonias, for it has been traditional to regard these cases as presenting with minimal or even absent physical signs.

Of the 19 cases with an *area of localized rales* and varying degrees of clinical illness, 14 had an abnormal radiograph (74%)—they were aspiration pneumonias (6), bacterial pneumonias (5), or pneumonias of viral or uncertain origin (3). Of the five patients with normal radiographs, one had influenza and in the remainder all investigations were negative.

A woman aged 23, with an area of localized rales, a normal radiograph, and negative investigations, fell ill some days after her husband, who had been the victim of, clinically, the same disease. He also had an area of rales at one base, and his investigations were likewise negative except for the radiograph, which showed a lobular opacity at the site where the rales had been heard. The fever of both patients settled without antibacterial therapy, and both were fit to return to work within two weeks. But, although the husband was by then symptom-free, it was some months before his radiograph returned to normal. It was thought that both had suffered from the same disease, possibly viral in origin, which had produced radiological changes in one and not in the other.

Only 7 of the 13 patients who presented with *bilateral and diffuse rales and rhonchi* and were diagnosed as cases of "pneumonia" had abnormal radiographs (54%), but this group includes the majority of patients with chronic bronchitis for whom reasons have been given for considering that the diagnosis of pneumonia was usually justifiable even though not radiologically proved. Of the seven patients with abnormal radiographs, six had aspiration pneumonias and one was a bronchial carcinoma.

The two patients with a *pleural rub* as the only physical sign both had developed aspiration pneumonias following infections of the upper respiratory tract, one proceeding to abscess formation and a spontaneous pneumothorax.

The three cases suspected on the basis of the clinical picture to have pneumonia, even though *no abnormal physical* signs were elicited, were all confirmed radiologically to have pneumonia (bacterial and aspiration).

The results of our investigations showed a fair correlation between the initial clinical classification and that finally revealed. Seven out of the nine cases of proved influenza were so diagnosed clinically, and the diagnosis of pneumonia was correct in 29 of the 37 cases where it was radiologically proved (78%).

In 63.7% of our cases no specific aetiological diagnosis could be established. The proportion of cases in which a specific diagnosis was made varied in the three clinical groups; it was highest in the "influenzas with chest complications" (36%), followed by the "pneumonias" (31%), and was lowest in "bronchitis" (13%). Of the 34 radiologically proved pneumonias from all three groups, the majority (61.7%) were non-specific aspiration pneumonias, 26.5% were bacterial, and 11.8% were virus pneumonias. A definite aetiological diagnosis was made in only 36.3% of the 80 cases, and was achieved by elaborate pathological investigations, but it was of interest to note that in only a few cases were the results of real practical value as a guide to management. The majority of patients recovered with the treatment that was given on clinical criteria, though the investigations suggested that some who were given antibacterial therapy might have recovered as quickly without it.

DISCUSSION

The investigation concerned the detailed clinical and pathological study of 80 cases of acute infective chest disease in the practice of eight practitioners on the outskirts of south-east London. It is appreciated that the number of cases was small, that the experiences are not representative of practice throughout the country, and that there were limitations in the investigations.

The subject provides many problems for discussion, but this is confined to those aspects to which especial consideration was given.

Aetiology

The importance of age in the aetiology of acute chest infections is shown in Fig. 3, which gives the age of 270 patients with acute chest infections in the practice of one

of us (J. F.) over the previous five years, and shows that 80% occurred in patients under 10 and over 50 years of age. The exclusion of children, who accounted for 40% of the 270 cases, from the present study, naturally limited the number of acute chest cases that were investigated from the practices concerned.

The study was made in a suburban community, where it is more difficult to trace the source of infective illness than in the country. Not only could infection be contracted locally, but, in most households, at least one member travelled daily to central London, and it was thought that many infections were contracted in this way or from contacts at work. Six patients, including two teachers, appeared to have been infected at school, and in 18 cases (20%) the probable source of infection was another member of the family.

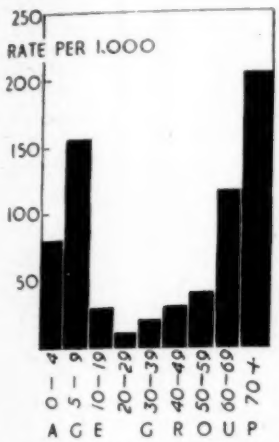


FIG. 3.—Incidence of acute chest infections in different age groups, shown as rate per thousand atendances. Figures from the practice of J. F., 1949–54.

The close association between upper and lower respiratory infections was confirmed, for 55 of the patients (68.8%) gave a history of an upper respiratory infection, either in the two weeks prior to the onset of their chest infection (43.8%) or occurring concurrently (25%).

From the investigations undertaken, it was possible to demonstrate a specific bacterial aetiology in only 17.5%, and a viral aetiology in 18.8%. In most cases the cause was a non-specific catarrhal infection. Some cases may have been secondary to primary infection with the virus of the common cold, and others may have been febrile catarrh (Stuart-Harris *et al.*, 1938) or acute respiratory disease, A.R.D. (Commission on Acute Respiratory Diseases, 1947). These two names describe a similar condition which is caused by the R1–67 virus (Hilleman and Werner, 1954), type 4 of the adenoid-pharyngeal-conjunctival (A.P.C.) group of viruses (Huebner *et al.*, 1954). Although primarily a cause of upper respiratory catarrhs, these viruses may cause bronchitis and pneumonia, and when the tests for their presence are more widely available it will be of interest to investigate the frequency with which they cause respiratory infections in this country.

That many of the cases should prove to be non-specific catarrhal infections was not surprising. Even in a series of pneumonias studied at Hammersmith Hospital, Crofton *et al.* (1951) were unable to demonstrate a specific aetiology in 45%, of which 59.5% had received no chemotherapy before admission. Prompt chemotherapy, which is given in the majority of acute chest infections, may eliminate bacteria before they appear in sufficient numbers for detection by the methods available, or may suppress the secondary infection of catarrhal conditions. But, whatever the explanation, the results of this study showed that, even with careful investigation, a specific aetiology can be demonstrated only for the minority of acute respiratory infections encountered in general practice to-day, and that the majority are non-specific catarrhal infections of largely unknown aetiology.

Clinical Classification

Established practitioners evolve their own terminologies for describing the acute respiratory infections with which they deal, but the new entrant will certainly experience "perplexity . . . in trying to take the nomenclature of the laboratory and classroom into the maze of undiagnosed respiratory disease in his practice" (Spence *et al.*, 1954). In view of the difficulties of clinical terminology, we classified our cases into one of three groups—"influenza with chest complications," "bronchitis," and "pneumonia"—and have given the criteria by which they were recognized. However, any such classification is certain to produce difficulties in deciding into which group a given case will fall, and this is paralleled by clinical practice, where a case which presents as one condition may by the following morning be clearly an example of another. But in the main there was a reasonable correlation between the separation of cases into three groups and the results of the investigations, and it appeared to be as simple and practical as any classification that we have seen proposed.

In the clinical classification, the importance and value of physical signs in the chest have been emphasized, although in recent years these have been subjected to criticism by the statistical studies of Fletcher (1952) and Schilling *et al.* (1955), who have shown the wide discrepancies which even expert physicians may make in their interpretation. The valuable work of these authors has emphasized the false claims or unwarranted deductions which a single observer may inadvertently make, and have shown that the discrepancy between two observers is greatest when assessing signs which lack clear definition. Our observations on physical signs were therefore all made by two observers, one of whom examined all the cases in the study, and we limited our records of abnormal signs to those that were definite.

The frequency and importance of abnormal physical signs were shown by their occurrence in 92% of the patients. Their distribution into the five groups already mentioned is shown in Table VI, where the relative incidence is compared with those found in the larger series of 270 cases observed by one of us (J. F.) over a five-year period. The figures from the two series are closely comparable and demonstrate the rarity of the signs of pulmonary consolidation in general practice to-day. These were present in only 5% and 8% of the two series, and in 11% of the radiologically proved pneumonias in the present study. The two most frequent groups of signs were an area of localized rales (33.7% and 52%) or generalized diffuse and bilateral adventitia of varying intensity (47.5% and 39%). The localized rales were persistent and usually maximal in one area only. The percussion note was sometimes impaired at the same site, and local radiological changes were present in 74%.

TABLE VI.—*Analysis of Abnormal Physical Signs in Chest in* 80 *Cases of Acute Chest Infections Studied in the Winter of* 1954–5 *Compared with those in* 270 *Cases Seen Between* 1950 *and* 1955

	80 Cases 1954–5. Adults Only	270 Cases 1950–5. All Ages
Consolidation	5%	8%
Localized rales	33·7%	52%
Diffuse bilateral adventitia	47·5%	39%
Pleural rub only	2·5%	1%
None	11·3%	—*

* This series was confined to cases with abnormal pulmonary signs.

It is not as easy to elicit abnormal physical signs in a bedroom of traditional English winter temperature as in a well-heated hospital ward, but physical signs are a valuable aid to the practitioner in his diagnosis and management of acute chest infections. They may confirm his suspicion of pulmonary disease, though their absence does not exclude it, and they may give an indication of whether the inflammation is localized or diffuse. Their exact interpretation may be difficult without radiography, but in conditions such as pleurisy, bronchitis, and asthma physical signs may reveal more than a radiograph.

Value of Investigations

Investigations were primarily undertaken in this study to determine the aetiology of a random series of acute chest infections, and these results have been discussed. A

secondary aim was to observe which of the investigations were of greatest help to the practitioner in the management of these cases and any special problems related to their performance in general practice. The three basic investigations of an acute chest infection are a radiograph, sputum examination, and blood picture, all of which can be carried out, if necessary, by a practitioner who has access to pathological and radiological services at his local hospitals. In the present study a blood count proved to be of least practical value, since 72% had normal white-cell counts. Leucopenia is suggestive but not conclusive of virus infection, and in the proved virus infections studied was less common than a normal white count. A leucocytosis suggests a bacterial infection, and therefore antibacterial therapy will be helpful; but our numbers were not sufficient to show whether the acute chest infections with leucocytosis recovered more quickly if given antibacterial therapy than if they were not.

It is often preached but seldom practised that sputum should be examined from all cases of pneumonia in general practice, but in spite of attempts to obtain samples early in the course of disease, from all cases, our results were disappointing, and the results of attempted bacteriological isolations from other sources even less so. Sputum examination is among the easier examinations for a practitioner to undertake, but our findings emphasize that satisfactory samples will be received by the laboratory only if the practitioner collects and delivers them himself. But in busy winter months or in rural practice it is obviously impracticable for him to do this in all cases. Furthermore, the present results show that, even if adequate samples of sputum are examined, the results will often be negative for significant pathogens.

Radiographs of the chest were the most helpful of the investigations. In acutely ill patients, or where diagnostic doubt existed, a domiciliary radiograph was of great value and saved ill patients from journeys to hospital for either admission or out-patient radiography. But in most cases it is possible to defer radiography until the acute phase of illness has been passed and then arrange for a radiograph at a local hospital or chest clinic during convalescence. The percentage of cases in this study which had a domiciliary radiograph was higher than is normally necessary, but that measure was undertaken as part of the investigation. The importance and value of the practitioner's access to local radiological facilities is well shown in the field of acute infections of the chest, for it enables him to improve his standards of diagnosis and treatment, it reduces the need for hospital beds, and is a means for detecting early cases of tuberculosis and carcinoma. It was also apparent during the study that a more economical use of films is made than when comparable cases are treated in hospital.

Our conclusion was that a practitioner must rely on clinical judgment to decide which of his cases of acute infective chest disease merit careful investigation, for it is clearly impracticable and impossible for him to investigate them all. Of the investigations, radiography is the most informative, and there should be good reason for not arranging for a radiograph at some stage of illness in the type of case with which this paper is concerned.

Treatment

The core of the problem of treatment of acute infective chest disease in general practice is deciding when antibacterial therapy should be given and, if so, in which form. It is not necessary or desirable to treat minor catarrhal infections which will recover without antibacterial agents, but a practitioner does not wish to prejudice his patient's recovery by failing to institute such treatment when necessary. It is therefore natural that the practitioner will err on the side of over-prescribing rather than under-prescribing, but the excess should not be an unreasonable one.

In most instances patients with acute infective chest diseases are treated at home. Of the present series only 5%, and in the larger series of 270 cases only 3.6%, were admitted to hospital. The proportion of cases admitted in different areas will depend on the facilities for home care, local investigative facilities, and the medical needs for hospital treatment, but in the area of study the proportion is small. Examination of the cases of "pneumonia" admitted to local hospitals during 1954–5 revealed that failure to respond to initial chemotherapy in the home, or the need for special hospital care in severely ill patients, were the two chief reasons for which their admission to hospital had been requested.

Of the main therapeutic problems which confront a practitioner, the decision whether or not an antibacterial agent is required is more difficult to make than which particular antibacterial agent should be used. Once it has been decided to give antibacterial treatment, we believe that there are only a few exceptions to the principle that all should initially be treated with penicillin or sulphonamides, or sometimes a combination of both. Exceptions include those patients who are so severely ill when first seen that a tetracycline drug seems to be indicated and patients who have a previous history of sensitivity to penicillin or sulphonamides. It is difficult to give exact indications for administering antibacterial agents, and when doubt exists it is probable that a practitioner will administer rather than withhold them. In general, the decision has to be made in the first instance on clinical evidence, and it is for this reason that we have stressed here the clinical presentation of the cases. The severity of the illness is the factor which most often influences a practitioner in deciding whether to give antibacterial therapy, but the physical signs, nature of the sputum, etc., provide useful guides to its need. In only a small proportion of cases in this series was treatment influenced by the investigations, and among the reasons was that the results were not known to practitioners for at least three days, except in the case of domiciliary radiography, where an answer could be obtained within twenty-four hours or less of the patient's first being seen. In only two cases was the sputum examination of value in the decision upon treatment, and these were *H. influenzae* infections which had not responded to initial penicillin. In most cases either no pathogenic organisms were isolated or the patient was improving satisfactorily on treatment already instituted by the time a positive result was received.

The therapy given to the patients in this study was in no way controlled or modified for the purposes of the investigation, and each practitioner gave to his cases the treatment which he would normally have considered appropriate. When the results were analysed, the finding of greatest interest was that almost half of the cases (45%) had recovered satisfactorily with symptomatic treatment only (Table VII);

TABLE VII.—*Treatment Given in 80 Cases of Acute Chest Infections in General Practice*

Therapy	No.	%
Non-specific (symptomatic treatment only)	36	45
Penicillin	22	28
Sulphonamides	9	11
Penicillin and sulphonamides	1	1
Tetracyclines (first choice)	4	5
" (second ")	8	10
	80	100

40% had been given penicillin or sulphonamides, and one of the tetracycline group was administered in 15%. Of those given a tetracycline, this was the original choice in 5%, one of whom was a man with chronic bronchitis already on another member of the same group of drugs as a long-term prophylactic, and the second refused injections; in 10% tetracyclines were prescribed because of a failure to respond to penicillin or sulphonamides. Of the 36 patients given only symptomatic treatment, the majority were "influenza with chest complications" (15) or "bronchitis" (13), but the group included some of the mild "pneumonias" (8).

The use and abuse of antibacterial agents in general practice is a much-discussed topic of the present day, and their

role in the treatment of acute respiratory infections often arises. We have no evidence to show whether the recovery of those patients given symptomatic treatment only would have been hastened with antibacterial treatment, nor whether some of the treated patients would have recovered as quickly without. Such a decision could have been reached only by studying a larger number of patients with a planned therapeutic trial, an undertaking which would be difficult to carry out under the conditions of general practice.

SUMMARY AND CONCLUSIONS

An account is presented of an investigation of 80 cases of acute infections of the chest, severe enough to confine the patients to bed at home, during the winter of 1954–5. The patients remained under the care of their practitioners and were investigated in their homes.

The difficulties of clinical nomenclature of acute chest infections are discussed and a simple classification, applicable to general practice, has been used to divide the cases into three clinical groups: "influenza with chest complications" (28%), "bronchitis" (20%), and "pneumonia" (52%). "Influenza with chest complications" was diagnosed only at times of known epidemic, and the main clinical distinction between "bronchitis" and "pneumonia" was the degree of constitutional disturbance, though cases with localized abnormal signs, irrespective of the degree of illness, were diagnosed as "pneumonia." Abnormal physical signs were present in 92% of the cases and their value in diagnosis and management is discussed.

As a result of detailed investigation, a specific bacterial aetiology was revealed for 17.5% and a viral aetiology for 18.8%, but the majority appeared to be non-specific catarrhal infections.

Radiography showed significant abnormalities in 45% of the cases, being highest (75%) in those with clinical "pneumonia."

Attempted bacteriological isolations were made from throat and pernasal swabs, sputum, and blood cultures, but, in spite of their collection early in the course of disease, positive isolations were made in only 16% of 212 samples, and in only 17.5% of the total number of cases were the results considered of aetiological significance. The pathogenic organisms most often isolated were *Str. pneumoniae*, *H. influenzae*, and *Staph. aureus* (coagulase-positive). No virus isolations were made from 67 gargles; examination of 70 pairs of sera showed diagnostic evidence of influenza B (8), influenza A (1), psittacosis (2), and elevation of the streptococcus MG titre in three cases with other evidence of virus pneumonia.

Routine haemoglobin estimations disclosed no cases of anaemia. Elevation of cold agglutinins to a significant titre was found only in patients with other evidence of virus pneumonia (though it is known that they may be raised in bacterial and other infections). Of 75 white-cell counts, 54 were normal, 3 were low, and 18 were raised. The three cases with leucopenia were all virus infections, but 12 other virus infections had normal white-cell counts.

No planned therapeutic trial was attempted, and each practitioner gave that treatment which he would normally have considered appropriate. It was found more difficult to decide which cases should be given antibacterial therapy than which antibacterial agent should be prescribed; once it had been decided to give antibacterial therapy there were few exceptions to the practice that all should first be given penicillin or sulphonamides. Symptomatic treatment only was given to 45% of the cases, 40% were given penicillin or sulphonamides, 5% had a tetracycline drug as the initial choice, and 10% were given a tetracycline drug after failure to respond to penicillin or sulphonamides. Of the cases 95% were treated at home.

There was a reasonable correlation between the initial clinical separation of the cases into the three main groups and the final diagnosis revealed by the investigations. Seven out of the nine proved cases of influenza were diagnosed clinically and the initial diagnosis of pneumonia was correct in 75% of those in whom it was radiologically proved. Of the proved pneumonias, 67.1% were non-specific aspiration pneumonias, the majority of which had been so diagnosed on clinical grounds.

The practical value of the investigations was small in comparison with the work involved in their execution. The most helpful measure was radiography, and the special value of domiciliary radiography in cases of diagnostic doubt or severe chest illness is stressed. Bacteriology was the second most helpful of the measures, although a high percentage of negative results were obtained. Although it involves extra labour for the practitioner, the only way to ensure that the laboratory receives a fresh and adequate sample of sputum for examination is for him to collect and deliver it himself. In those cases where pathogenic bacteria were isolated the patients were usually better from the treatment already given by the time the results were known; in only two instances, of *H. influenzae* infection, were the results of practical value as a guide to specific therapy. In a number of cases where the clinical response to antibacterial therapy appeared to be significant, the negative bacterial results might be considered to have indicated that that form of treatment was unnecessary; this may have been so in some instances, but in others it may have been due to a failure of technique in collecting and culturing the samples by routine methods.

The white-cell counts were of limited value, as 75% were within the normal range. The three cases with a leucopenia were all proved to have virus infections, but it was more common to find a normal count in those in whom the diagnosis of virus infection was later proved. Leucocytosis suggested a bacterial infection, but this was not always confirmed bacteriologically; it also suggested the cases which would benefit from antibacterial therapy, but our numbers were not sufficient to show whether the cases with leucocytosis recovered more quickly with antibacterial therapy than without it. The main value of the E.S.R., based on previous experience, rather than the results obtained in this investigation, was that persistent elevation after clinical recovery from an acute chest illness may be a useful pointer that the case requires careful investigation.

Virus tests were of the least practical value, mainly because the results are not known to a practitioner for at least four weeks from the start of the illness. They were, however, of clinical interest in the present investigation in proving the diagnosis of influenza in nine cases, revealing two unsuspected cases of psittacosis, and providing supportive evidence for the diagnosis of virus pneumonia.

We wish to express our thanks to the many people who made this investigation possible, particularly to the patients for their co-operation, and to their doctors, whose names have been given,

for the help they gave us and the detailed case records which they kept. To Dr. L. L. Griffiths and Dr. J. Keall and their technical staffs, especially Mr. W. J. Hatcher, we are indebted for the pathological investigations that were carried out at Farnborough, Bromley, and Beckenham Hospitals; and to Dr. A. C. Glendenning and his staffs at Bromley and Beckenham Hospitals for the radiology. We are grateful to Dr. E. R. Mitchell for help with the transport of the garglings and to Dr. L. A. Hatch, of the Virus Reference Laboratory, Central Public Health Laboratory, Colindale Avenue, for the virus studies. For help with the preparation of the manuscript we wish to thank Dr. N. S. Plummer. The work was carried out while one of us (A. B. S.) held the appointment of senior medical registrar in the Bromley Group, made jointly by Guy's Hospital and the South-east Metropolitan Regional Hospital Board.

REFERENCES

Bedson, S. P. (1955). In *Virus and Rickettsial Diseases* by S. P. Bedson, A. W. Downie, F. O. MacCallum, and C. H. Stuart-Harris, 2nd ed., p. 125. Arnold, London.
Commission on Acute Respiratory Diseases (1947). *Medicine (Baltimore)*, **26**, 441.
Crofton, J. W., Fawcett, J. W., James, D. G., Scadding, J. G., Macrae, A. D., and Marmion, B. P. (1951). *British Medical Journal*, **2**, 1368.
Fletcher, C. M. (1952). *Proc. roy. Soc. Med.*, **45**, 577.
Fry, J. (1955). M.D. Thesis, University of London.
Hilleman, M. R., and Werner, J. H. (1954). *Proc. Soc. exp. Biol. (N.Y.)*, **85**, 183.
Huebner, R. J., Rowe, W. P., Ward, T. G., Parrott, R. H., and Bell, J. A. (1954). *New Engl. J. Med.*, **251**, 1077.
Logan, W. P. D. (1953). G.R.O. Studies in Medical and Population Subjects, No. 7, p. 77. H.M.S.O., London.
Pemberton, J. (1949). *British Medical Journal*, **1**, 306.
Reid, L. McA. (1954). *Lancet*, **1**, 275.
Scadding, J. G. (1952). In *Diseases of the Chest*, edited by Sir G. Marshall and K. M. A. Perry, **1**, 60. Butterworth, London.
Schilling, R. S. F., Hughes, J. P. W., and Dingwall-Fordyce, I. (1955). *British Medical Journal*, **1**, 65.
Spence, Sir J., Walton, W. S., Miller, F. J. W., and Court, S. D. M. (1954). *A Thousand Families in Newcastle-upon-Tyne*, pp. 42, 58. Oxford Univ. Press, London.
Stuart-Harris, C. H. (1953). *Influenza*, p. 93. Arnold, London.
—— Andrewes, C. H., and Smith, W. (1938). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 228
Taylor, S. (1954). *Good General Practice*, p. 399. Oxford Univ. Press, London.

ARGENTAFFIN CARCINOMA OF ILEUM WITH RAISED SERUM 5-HYDROXYTRYPTAMINE

REPORT OF A CASE

BY

DAVID DUNCAN, M.B., F.R.C.S.Ed.
Senior Casualty Officer, Cumberland Infirmary, Carlisle

JEAN D. GARVEN, Ph.D., B.Sc.
Formerly of Pharmacological Laboratory, University of Edinburgh

AND

JAMES L. GIBBONS, M.B., M.R.C.P., D.P.M.
Medical Registrar, Maudsley Hospital, London; lately of Cumberland Infirmary, Carlisle

Gastro-intestinal argentaffin carcinoma has lately been recognized as an endocrine growth which may cause flushing attacks and cyanosis, and perhaps stenosis of the pulmonary valve of the heart. The existence of this syndrome was suggested by Biörck *et al.* (1952), who described the post-mortem discovery of argentaffin carcinoma of the ileum in a patient who had complained of cyanosis, flushing attacks, dyspnoea, abdominal pain, and diarrhoea, and who had a pulmonary valvular stenosis. In the same year similar features were recognized by Waldenström and Ljungberg in a patient who had had an argentaffin carcinoma excised in 1944, and by Björkman in another case at necropsy. The observation of changes in skin colour and of flushing attacks led to laparotomy in two further patients, and argentaffin carcinoma was found. To a detailed description of these five cases Thorson *et al.* (1954) have added one from their hospital records and have considered three described by Isler and Hedinger (1953), two by Rosenbaum *et al.* (1953), and five reports from earlier literature. Other probable cases have been described after death by Ratzenhofer and Lembeck (1954), Branwood and Bain (1954), Jenkins and Butcher (1955), and Fraser (1955), while Page *et al.* (1955) mention a patient with characteristics of the same syndrome.

We have recently encountered a patient in whom, following resection of a stenosing tumour of the ileum, the probable histological diagnosis was postulated on the basis of the reddish-blue colour of the patient's skin. Affinity of the tumour cells for silver was not demonstrated, but we believe that the finding of raised levels of serum 5-hydroxytryptamine (5-H.T.) and urinary 5-hydroxyindoleacetic acid (5-H.I.A.A.) confirms that the tumour originated from argentaffin cells.

Case Report

A man aged 23 was admitted to hospital in January, 1955, with intestinal obstruction and a history of flushing attacks and cyanosis.

Skin Colour.—Since the age of 18 years his face had become red. It felt warm during almost every meal, and this flushed feeling usually subsided in about half an hour. In the past year there had also been some blueness of the face and hands out of doors, and he attributed this to the cold. He had become used to his colour, which caused him no concern. On examination at rest the face was red with a bluish tinge. Dilated capillaries were easily seen with the aid of a loupe. There was no clubbing of the fingers.

Abdominal Condition.—For ten months he had suffered repeated bouts of spasmodic central abdominal pain lasting about 24 hours, and accompanied by vomiting. At these times he could palpate a swelling in the lower abdomen and could feel it move. The attacks would often subside after a series of loose black stools, but there was no diarrhoea at other times. There had been some flatulence and borborygmi, and heartburn had been troublesome. His appetite was fair and he was not aware of any change in weight. For two weeks before admission he had suffered pain every day, and in the last 36 hours he had vomited repeatedly. On examination there was no abdominal distension. During a spasm of pain a tender, mobile, sausage-shaped swelling was palpated in the hypogastric region, and there was transient visible peristalsis in the same area. When the spasm had subsided the abdomen appeared normal.

Laparotomy revealed a stricture of the ileum 60 cm. from the ileo-caecal valve, associated with contracted mesentery containing two enlarged lymph nodes. In the liver were numerous hard nodules up to 2 cm. in diameter. The thickened mesentery and glands were excised with the stricture, and continuity of the ileum was restored by side-to-side anastomosis.

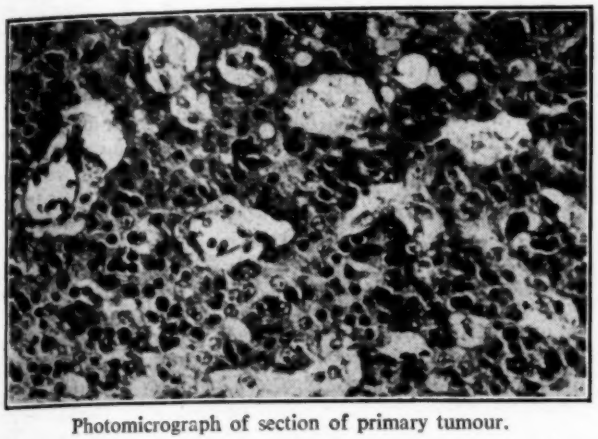
Investigations

Pathology.—The specimen consisted of a segment of small intestine with obstruction caused by a ring stricture. Above this there was distended loop of hypertrophied ileum, and below was a segment of collapsed bowel. In the adjacent mesentery the lymph nodes were enlarged and had obviously been invaded by secondary tumour. Microscopically the muscle wall was invaded by sheets of eosinophilic cells with poorly demarcated outlines and pale-staining nuclei with a well-marked membrane. In some areas a pseudo-adenomatous arrangement was present (see Fig.). The sections resembled Kultschitzky-cell carcinoma more closely than adenocarcinoma, but affinity of the cells

for silver could not be demonstrated. The lymph nodes were invaded by sheets of cells similar to those of the primary growth in the bowel wall.

Blood.—Haemoglobin, 72%; red cells, 4,310,000. The blood contained no sulphaemoglobin or methaemoglobin.

Serum 5-Hydroxytryptamine.—The patient's serum 5-H.T. content was estimated from blood collected between flushing attacks nine days after operation, and was found to be 3 μg. per ml., almost ten times the highest value obtained from six normal human subjects by Cottrell *et al.* (1955), who recorded the following results: 0.05, 0.1, 0.175, 0.182, 0.26, and 0.354 μg. of 5-H.T. per ml. of serum. The method used throughout was that of Amin *et al.* (1954).



Photomicrograph of section of primary tumour.

Urinary 5-Hydroxyindoleacetic Acid.—The 5-H.I.A.A. content of a 24-hour sample of the patient's urine was estimated at approximately 80 mg., or eight times the highest normal value recorded by Titus and Udenfriend (1954), who found 5–10 mg. of 5-H.I.A.A. in 24 hours.

Heart.—The heart rate was 74 and the blood pressure 105/65. No murmur was detected on auscultation. An electrocardiogram showed clockwise rotation of a semi-vertical heart. The P wave in lead II was 3.5 mm. tall. Radiological examination showed that the heart was normal in size and shape. There was no right ventricular enlargement and no abnormality of the pulmonary conus or pulmonary artery to suggest pulmonary stenosis. The vascularity of the lung fields was within normal limits. Examination at another hospital within the previous three months had shown a coarse systolic murmur over the xiphoid process. A phonocardiogram had indicated a systolic murmur at the apex and a short diastolic murmur over the lower left sternal border. A radiologist suspected pulmonary stenosis. Barium-meal and barium-enema examinations had been negative, and a "follow-through" examination had been advised.

Progress

Peristalsis returned within 36 hours after operation, and the bowels began to move four or five times daily.

The red colour of the face persisted and the patient continued to experience flushing. Walking 100 yards caused him no distress, but produced a deep uniform cyanosis of the whole of the face, head, and neck, and, to a less extent, of the limbs and trunk. After a few minutes at rest pink thumb-nail patches appeared in the blue skin of the face and chest and persisted as the cyanosis decreased.

Five months later he was reported to have been at work as an electrician for three months and was feeling well. The changes in skin colour had continued.

Discussion

5-Hydroxytryptamine

This was first detected as "enteramine" (Vialli and Erspamer, 1933), which was assumed to originate in the Kultschitzky cells of gastro-intestinal mucosa (Erspamer, 1940). It was later isolated from blood as "serotonin" (Rapport *et al.*, 1948), and was synthesized (Hamlin and Fischer, 1951).

Feyrter suggested that the scattered gastro-intestinal argentaffin cells might possess an endocrine functional unity, and pharmacological assay of argentaffin tumours was attempted by Feyrter and Unna (1936), and by Selberg (1941), but with inconclusive results. Lembeck (1953) obtained a post-mortem specimen of argentaffin tumour for assay, and found at least 2.5 mg. of 5-H.T. per g. of fresh tumour tissue. He detected also another smooth-muscle-stimulating substance which was not identified. Similar evidence of the high 5-H.T. content of argentaffin tumour tissue was found by Page *et al.*, who estimated 0.9 mg. of 5-H.T. per g. from a biopsy specimen.

Thorson *et al.* suggested that excessive secretion of 5-H.T. by argentaffin tumours might be the cause of the syndrome which they had observed. Blood collected from two patients during flushing attacks was examined by Pernow and Waldenström (1954), who found 12 μg. and 15 μg. of 5-H.T. per ml. of serum, and compared these figures with normal levels of 0.03–0.2 μg. per ml. recorded by Erspamer (1954). They concluded that their results could be attributed to secretion of 5-H.T. by metastases, since the primary tumour had been removed in each case.

In normal subjects a proportion of 5-H.T. is excreted in the urine as 5-H.I.A.A. and has been estimated at 5–10 mg. of 5-H.I.A.A. daily (Titus and Udenfriend, 1954). Urine from three patients with argentaffin tumours contained 65–350 mg. of 5-H.I.A.A. a day, although only one of these patients is known to have presented the characteristics of the syndrome (Page *et al.*, 1955). Reviewing 157 contributions to the literature, Page (1954) states that consideration of the functional significance of 5-H.T. depends on conjecture alone. Possible roles include control of peristalsis, stimulation of glandular secretion, antidiuretic action, some part in vascular homoeostasis and in nerve metabolism, and regulation of the excitatory nerves of the heart. 5-H.T. is present in blood platelets and may be released from platelet plugs at sites of vascular injury. It may thus be concerned in the effects of coronary thrombosis, pulmonary embolism, and traumatic shock.

The Primary Tumour

Argentaffin-cell tumours may arise in the stomach, intestine, pancreas, or gall-bladder, and are the commonest new growths of the appendix and of Meckel's diverticulum. Willis (1948) finds the majority are histologically distinctive and can be identified without the unreliable silver-staining test. He decries the term "carcinoid" because many of them are invasive and metastasizing growths, and prefers to call them argentaffin or Kultschitzky-cell carcinomas. In the small intestine they may form multiple nodules or plaques, or single growths may encircle the bowel and cause stenosis. Spread to mesenteric lymph nodes and liver is frequent, and remote metastases may appear in lung, kidney, adrenal, brain, and skin. Isler and Hedinger mention a metastasis in a rib. Some of these tumours show very slow progress: one patient described by Thorson *et al.* had abdominal symptoms for 20 years before the obstruction caused by an argentaffin carcinoma of the ileum was relieved by a lateral anastomosis, leaving the tumour undisturbed. The patient survived 16 years after this operation.

It has been suggested that the argentaffin granules in Kultschitzky cells are produced by the interaction of 5-H.T. and formalin, which produces also the yellow colour of carcinoid tumours (Ratzenhofer and Lembeck, 1954). These authors believe that failure of silver staining may be attributable to autolysis when formalin fixation is delayed after death or after removal of the tumour at operation. An interval of not more than two hours elapsed between excision of our specimen and its immersion in 10% formalin

solution. The cut surfaces of the primary and secondary tumours in the fixed specimen were greyish white and not yellow.

Hepatic Metastases

These have been present in all cases of the syndrome (see Table). There may be a critical level of serum 5-H.T. beyond which features of the syndrome appear, related to a bulk of argentaffin tissue attained only by the development of multiple hepatic metastases. If the liver normally modified the amount of 5-H.T. passing from portal to peripheral blood it might be suggested that secondary growths situated in the liver could secrete large amounts of 5-H.T. directly into the systemic blood stream.

Cutaneous Vascular Phenomena

Some change in skin colour is reported in all cases, varying from patches of red, mauve, blue, and purple-grey to permanent cyanosis. If the skin changes depend on increased serum 5-H.T. they may indicate the age of the tumour. In our patient this would be at least five years. Experimentally, intradermal injection of 5-H.T. may cause a red, often morbilliform, reaction without itching or wealing (Reid and Rand, 1952).

The association of flushing with meals has been observed by several patients. Perhaps the flush signals a sudden increase in serum 5-H.T., the response of argentaffin cells to a humoral reflex following the entry of food to the stomach. It has been calculated that the serum 5-H.T. levels found by Pernow and Waldenström in patients during flushing indicate the instantaneous presence in the blood of up to 30 mg. of 5-H.T. In normal subjects, however, side-effects prevent the instantaneous injection of more than 1 mg. of 5-H.T., and experimental infusion of 5-H.T. in these subjects does not cause flushing (Page *et al.*, 1955).

Cyanosis in this syndrome may appear years before signs of congestive heart failure, and in no case has the haemoglobin exceeded 100%. The blue colour, therefore, cannot be attributed to pulmonary stenosis, because the cyanosis of pure pulmonary stenosis is a late feature associated with congestive heart failure, while the cyanosis of pulmonary stenosis with patent foramen ovale results from the shunt of blood from right to left auricles and is associated with anoxaemia and polycythaemia.

Other Effects

Dyspnoea.—The infusion of 5-H.T. in man may cause a short period of hyperpnoea with exaggerated respiratory movements and complaint of difficulty in breathing (Page). Three patients described by Thorson *et al.* had expiratory stridor and dyspnoea during flushing attacks.

Effects on the Heart.—Signs of an organic lesion are a late feature of the syndrome. One patient described by Thorson *et al.* had no heart murmur at first but a harsh systolic murmur 14 months later; another had a murmur and E.C.G. evidence of right heart strain, but no valve lesion was found at necropsy. When affected, the pulmonary valve usually showed narrowing of the valve ring and partial fusion and fibrosis of the cusps. Thorson *et al.* remark, however, that the degree of stenosis was slight and that they would not have expected it to offer much resistance in otherwise normal persons. Yet a common finding was dilatation and hypertrophy of the right ventricle. Tricuspid incompetence was another feature, and in the first patient described by Biörck *et al.* the regurgitant flow was so great that a catheter could not be introduced into the right ventricle. Experimental infusion of 5-H.T. causes transient pulmonary vasoconstriction with high right ventricular pressure (Page). Repeated release of large amounts of 5-H.T. from argentaffin tumour tissue might be expected to cause repeated pulmonary vasoconstriction and secondary pulmonary hypertension. Whatever the cause of the heart lesions, the time over which it acts is evidently an important factor. Physical changes may follow the functional effects.

Abdominal Pain and Diarrhoea.—Before resection of a tumour in the bowel, pain and diarrhoea might result from recurrent subacute obstruction or from recurrent incipient intussusception. Alternatively, they might be caused before or after operation by high serum levels of 5-H.T. When subjected to barium-meal examination most of these patients have shown intestinal hurry. Normal individuals injected with 5-H.T. may complain of abdominal pain and a desire to defaecate (Page, 1954).

Diagnosis and Treatment

Diagnosis tends to be delayed. Even with a stenosing tumour of the small intestine, obstructive symptoms are late because the bowel content is fluid. Barium-meal examination confirmed the lesion in one patient described by Thorson

Summary of Recorded Cases

Author	Skin Colour	Flushing	Dyspnoea	Abdominal Pain	Diarrhoea	Histology	Primary Site	Hepatic Metastases	Heart Murmur	P.M. Pulmonary Valve Lesion
Cassidy (1930) ..	Red, mauve	Present	Present		Present	Columnar carcinoma	Not found	Present	Present	Stenosis
Arnett and Long (1931)	Bluish red		,,		,,	Adenocarcinoma	Pancreas	,,	,,	,,
Scholte (1931) ..	Red, blue		,,		,,	Carcinoid	Ileum	,,	,,	,,
Cassidy (1934) ..	Red	Present		"Discomfort"		Carcinoma	Stomach	,,	None	Not reported
Currens *et al.* (1945)	Blue			Present	Present	,,	Ileum	,,	Present	Stenosis
Biörck *et al.* (1952)	Red, blue	Present	Present	,,	,,	Carcinoid	,,	,,	,,	,,
Isler and Hedinger (1953)	,, ,,			,,	,,	,,	Jejunum	,,	,,	,,
	,, ,,		Present	,,	,,	,,	Ileum	,,	,,	,,
	Blue					,,	,,	,,	,,	,,
Rosenbaum *et al.*, (1953)	Purple-grey					,,	,,	,,		,,
	,, ,,					Adenocarcinoma	Hepatic bile ducts			,,
Thorson *et al.* (1954)	Red	"Heat waves"	Present	Present	Present	Carcinoid	Ileum	Present	None	,,
	Red, blue	Present	,,	,,	,,	,,	,,	,,	Present	(Patient alive)
	,, ,,	,,	,,	,,	,,	,,	Small intestine	,,	,,	,, ,,
	,, ,,	,,		"Discomfort"	,,	,,	Not found	,,	,,	Not reported
	,, ,,	,,		Present	,,	,,	Ileum	,,	,,	None found
Ratzenhofer and Lembeck (1954)	Cyanosis		Present	,,	,,	,,	Jejunum	,,		Not reported (but "tricuspid incompetence")
Branwood and Bain (1954)	Red, blue	Present	,,		,,	,,	Ileum	,,	Present	Stenosis
Jenkins and Butcher (1955)	,, ,,				,,	Argentaffinoma	Caecum	,,	,,	None found
	"Malar flush"		Present		,,	,,	Ileum	,,	,,	Stenosis
Fraser (1955) ..	Red, purple			Present	,,	Carcinoid	Caecum	,,		
Duncan, Garven, and Gibbons	Red, blue	Present	Absent	,,	,,	Argentaffin-cell carcinoma	Ileum	,,	None	(Patient alive)

et al., but was not helpful in other reported cases. The estimation of urinary 5-H.I.A.A. or serum 5-H.T. is not a routine measure, but raised values either before operation or without it would confirm a diagnosis of argentaffin carcinoma. A surgeon possessing this information might attempt more radical treatment than would be justifiable for widespread adenocarcinoma.

The slow progress of some of these cases makes it seem reasonable to resect the primary tumour and accessible metastases, to relieve obstruction, and to reduce the amount of tissue producing 5-H.T. One patient of Thorson *et al.* was still alive eight years after such a resection. Experimentally the vascular response to 5-H.T. is modified by drugs. Lysergic acid diethylamide (L.S.D.) specifically inhibits the effects of 5-H.T. on blood vessels of perfused rabbit's ear in concentrations of less than one in ten million; dihydroergotamine methane sulphate is another active antagonist (Gaddum *et al.*, 1955), and anti-5-H.T. effects are claimed also for chlorpromazine (Gyermek, 1955). In man, doses of L.S.D. around 30 μg. cause intoxication with traits suggestive of schizophrenia (Stoll, 1949), but L.S.D. or other antagonists might have therapeutic value if they were found to prevent flushing attacks and pulmonary hypertension.

Summary

A case of argentaffin carcinoma of the ileum with hepatic metastases and a serum 5-hydroxytryptamine level amounting to at least ten times the normal is described. 5-H.T. originates in the argentaffin cells of gastro-intestinal mucosa, is a normal constituent of the blood platelets, and appears in the urine as 5-hydroxyindoleacetic acid. It is produced in excess by tumours of argentaffin cells, and may be associated with a syndrome comprising flushing attacks, cyanosis, dyspnoea, abdominal pain, and diarrhoea, and secondary pulmonary hypertension.

APPENDIX

Serum 5-Hydroxytryptamine.—The patient's serum, which had been frozen for transport, was stored at −17° C., and three days later was thawed at room temperature. Duplicate samples of 2 ml. were placed in clean dry flasks. A third sample of 1.5 ml. of serum was added to 1 μg. of 5-H.T. base in 0.2 ml. of saline in a third flask.

Extraction.—Twenty volumes of acetone was added to each sample, which was shaken and then kept at 5° C. for one hour before filtering. Each precipitate was washed twice with 10 ml. and once with 5 ml. of 95% acetone; then the acetone filtrate and washings were evaporated almost to dryness, under reduced pressure at 35° C. To each sample 1 ml. of water was added before successive extractions with 15 ml. and 10 ml. of petroleum ether to remove lipids. The aqueous residues had a creamy yellow colour. They were evaporated to dryness and stored overnight at −17° C.

Assay.—The isolated atropinized oestrous uterus of the rat was used for assay of the specimens in terms of 5-H.T. base, with a sample of 5-H.T. creatinine sulphate supplied through the courtesy of Upjohn Laboratories, Kalamazoo, Michigan. The duplicate extracts were estimated to contain 3.2 μg. and 2.8 μg. of 5-H.T. base per ml. of serum respectively, and from the third sample 90% of the added 5-H.T. was recovered.

Specificity Test.—The uterus preparation was treated with L.S.D., which is a specific antagonist for 5-H.T. on this tissue (Gaddum, 1953). The contractions subsequently caused by the serum extracts and by 5-H.T. were similarly reduced, so the activity of the serum extracts was attributed to 5-H.T.

Urinary 5-Hydroxyindoleacetic Acid.—The sample was collected two weeks after operation and was stored in a frozen state for three months before analysis. The total volume was 815 ml.

Method.—A 400-ml. aliquot was extracted by the method of Erspamer (1955), and semi-quantitative estimation of the 5-H.I.A.A. content was made by comparison of the intensity of coloured spots given by the extract and by known quantities of 5-H.I.A.A. on paper chromatograms sprayed with *p*-dimethylaminobenzaldehyde in acid ethanol solution (1 g. of *p*-D.M.A.B.A. dissolved in 30-ml. mixture of equal volumes of concentrated hydrochloric acid and ethanol). Separate chromatograms were developed with *n*-butanol: 30% methylamine (8:3), *n*-butanol saturated with $\overline{N}$-HCl, and the organic phase of a mixture of *n*-butanol: acetic acid: water (4:1:5).

ADDENDUM.—In a recent publication Snow *et al.* (1955) have described three patients presenting with flushing and hepatomegaly. Increased amounts of blood 5-H.T. and urinary 5-H.I.A.A. were demonstrated in each case. In one the primary tumour was found in a Meckel's diverticulum, and in another in the stomach. Dosage with L.S.D., "Bol 148" (a derivative of L.S.D.), and ergotamine tartrate did not prevent flushing.

In another patient Goble *et al.* (1955) have shown that blood from the pulmonary artery contained more 5-H.T. than peripheral blood. The primary tumour was in the ileum, and there were signs of tricuspid stenosis. 5-H.T. antagonists were given without benefit, but temporary relief of flushing and dyspnoea was achieved by intravenous administration of colloidal radioactive gold, which is concentrated in the liver.

We are indebted to Dr. T. B. B. Crawford, of the Pharmacological Laboratory, University of Edinburgh, for the urinary 5-H.I.A.A. estimation; Dr. J. S. Faulds, of Cumberland Infirmary, for the pathologist's report; Dr. C. D. Anderson, of the Western Infirmary, Glasgow, for notes from his records; and to Professor J. H. Gaddum and Mr. R. M. Hill for advice and assistance in preparing this paper.

REFERENCES

Amin, A. H., Crawford, T. B. B., and Gaddum, J. H. (1954). *J. Physiol. (Lond.)*, **126**, 596.
Arnett, J. H., and Long, C. F. (1931). *Amer. J. med. Sci.*, **182**, 212.
Biörck, G., Axén, O., and Thorson, A. (1952). *Amer. Heart J.*, **44**, 143.
Branwood, A. W., and Bain, A. D. (1954). *Lancet*, **2**, 1259.
Cassidy, M. A. (1930). *Proc. roy. Soc. Med.*, **24**, 139.
—— (1934). Ibid., **27**, 220.
Cottrell, A. R., Sharman, D. F., and Sullivan, F. M. (1955). Unpublished work.
Currens, J. H., Kinney, T. D., and White, P. D. (1945). *Amer. Heart J.*, **30**, 491.
Erspamer, V. (1940). *Arch. exp. Path. Pharmak.*, **196**, 343, 366, 391.
—— (1954). *Ciba Foundation Symposium on Hypertension*, p. 78. London.
—— (1955). *J. Physiol. (Lond.)*, **127**, 118.
Feyrter, F., and Unna, K. (1936). *Virchows Arch. path. Anat.*, **298**, 187.
Fraser, I. (1955). *Lancet*, **2**, 174.
Gaddum, J. H. (1953). *J. Physiol. (Lond.)*, **121**, 15.
—— Hameed, K. A., Hathway, D. E., and Stephens, F. F. (1955). *Quart. J. exp. Physiol.*, **40**, 49.
Goble, A. J., Hay, D. R., and Sandler, M. (1955). *Lancet*, **2**, 1016.
Gyermek, L. (1955). *Lancet*, **2**, 724.
Hamlin, K. E., and Fischer, F. E. (1951). *J. Amer. chem. Soc.*, **73**, 5007.
Isler, P., and Hedinger, C. (1953). *Schweiz. med. Wschr.*, **83**, 5.
Jenkins, J. S., and Butcher, P. J. A. (1955). *Lancet*, **1**, 331.
Lembeck, F. (1953). *Nature (Lond.)*, **172**, 910.
Page, I. H. (1954). *Physiol. Rev.*, **34**, 563.
—— Corcoran, A. C., Udenfriend, S., Sjoerdsma, A., and Weissbach, H. (1955). *Lancet*, **1**, 466.
Pernow, B., and Waldenström, J. (1954). Ibid., **2**, 951.
Rapport, M. M., Green, A. A., and Page, I. H. (1948). *J. biol. Chem.*, **174**, 735.
Ratzenhofer, M., and Lembeck, F. (1954). *Z. Krebsforsch.*, **60**, 169.
Reid, G., and Rand, M. (1952). *Nature (Lond.)*, **169**, 802.
Rosenbaum, F. F., Santer, D. G., and Claudon, D. B. (1953). *J. Lab. clin. Med.*, **42**, 941.
Scholte, A. J. (1931). *Beitr. path. Anat.*, **86**, 440.
Selberg, W. (1941). *Klin. Wschr.*, **20**, 1271.
Snow, P. J. D., Lennard-Jones, J. E., Curzon, G., and Stacey, R. S. (1955). *Lancet*, **2**, 1004.
Stoll, W. A. (1949). *Schweiz. med. Wschr.*, **79**, 110.
Thorson, A., Biörck, G., Björkman, G., and Waldenström, J. (1954). *Amer. Heart J.*, **47**, 795.
Titus, E. O., and Udenfriend, S. (1954). *Fed. Proc.*, **13**, 411.
Vialli, M., and Erspamer, V. (1933). *Z. Zellforsch.*, **19**, 743.
Willis, R. A. (1948). *Pathology of Tumours*, p. 414. London.

SERIAL BIOPSY IN ULCERATIVE COLITIS

BY

S. C. TRUELOVE, M.D., M.R.C.P.
Assistant Physician, Nuffield Department of Clinical Medicine

A. R. HORLER, M.D., M.R.C.P.
Formerly Graduate Assistant, Nuffield Department of Clinical Medicine

AND

W. C. D. RICHARDS, M.B., B.S.
Graduate Assistant, Department of Pathology
(From the Radcliffe Infirmary, Oxford)

[WITH SPECIAL PLATE]

A recent therapeutic trial showed that patients treated with cortisone were nearly three times as likely to go into clinical remission as patients in a control group not receiving cortisone (Truelove and Witts, 1954). However, some workers have considered that corticotrophin (A.C.T.H.) and cortisone may check the bloody diarrhoea of ulcerative colitis without modifying the underlying diseased colon. For this reason we have devised a method which permits us to examine the histological changes in the mucosa of the rectum and sigmoid colon during the course of treatment with corticotrophin and cortisone.

In order to study these changes we decided to use a special instrument which would enable a biopsy to be made under direct vision through a sigmoidoscope and with minimal trauma to the patient. Mr. Richard Salt, chief technician to the Nuffield Professor of Anaesthetics, has made us such an instrument. An essential principle is one employed in the Wood gastric biopsy tube (Wood *et al.*, 1949), in that we rely on sucking a small knuckle

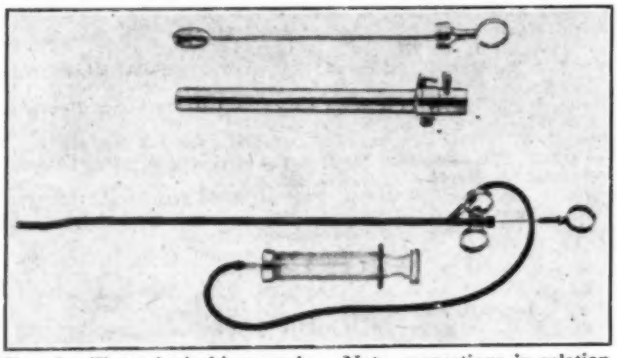


FIG. 1.—The colonic biopsy tube. Note proportions in relation to sigmoidoscope above.

of mucosa into a hole and then cutting it off cleanly with a sharp blade. The size of the hole determines the depth of the biopsy, and we have worked with a size which takes the biopsy down to the muscularis mucosae.

The Colonic Biopsy Tube and its Use

The apparatus used for biopsy (Figs. 1 and 2) is a rigid metal tube with a head which is slightly offset from the body. The head carries the cutting mechanism, which consists of a blade fashioned from a safety-razor blade operating with the edge obliquely set to the line of the instrument so that it has a guillotine action. (A biopsy knife made from a safety-razor blade has already been used by our colleague Dr. John Badenoch in an intestinal biopsy tube which he is developing in association with Mr. Richard Salt; we are grateful to him for permitting us to make use of this method.) The blade is attached to a sliding member in such a way that the edge is held in light pressure against the casing and a clean cut is thus assured. The blade carriage is operated by means of a fine steel tube which runs down inside the main tube and passes out through an airtight rubber gland into a ring for thumb or finger. This inner tube is rigid lengthwise but sufficiently flexible in lateral movement to permit the head to be offset as described. At the tail end of the instrument the main tube is fitted with a side tube to which a 20-ml. syringe for applying suction is attached by a short length of rubber tubing. The instrument is made an appropriate length for the particular sigmoidoscope used. In the present study we have used one suitable for a short (8 in.=20 cm.) sigmoidoscope.

A general sigmoidoscopic examination is made and a site selected for biopsy. In the present study we have taken all the samples at approximately 6 in. (15 cm.) from the anal margin. The lens at the end of the sigmoidoscope is removed, and the biopsy tube is inserted through the sigmoidoscope and the flat face of its head placed against the selected site. An assistant then withdraws the piston of the syringe, and on feeling resistance due to the mucosa plugging the hole in the head of the instrument he signals to the examiner, who operates the blade. The tube is then withdrawn, the end of the head unscrewed, and the biopsy specimen removed by flushing the instrument through with saline solution. The specimen is placed immediately into 10% neutral formol saline for histological examination.

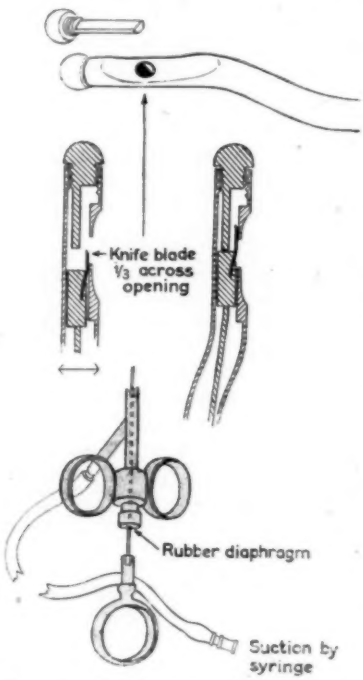


FIG. 2.—Details of colonic biopsy tube.

When using the biopsy tube for patients with severe ulcerative colitis the mucosa may be obscured by a profuse discharge of liquid faeces, blood, pus, and mucus. We have overcome this difficulty by using a suction irrigator (Fig. 3), likewise designed and built by Mr. Salt and based on a suction irrigator for use in dental surgery described by Boston and Macintosh (1939). It consists of two tubes joined along their lengths. One is a fine stainless steel tube fitted with a nozzle and covered with a rubber sheath which projects beyond the nozzle, through which a fine jet of warm saline is driven by means of a Higginson's syringe. The other tube, of much larger bore and made of rubber, is coupled to a suction apparatus with a foot control (Saher and Salt, 1943). The conjoined tubes are passed up the sigmoidoscope and simultaneous irrigation and suction are carried out. A clear view of the mucosa can be obtained by this technique, and we have observed nothing to suggest damage even to an acutely inflamed colon.

Below we report the findings in two patients with ulcerative colitis treated with corticotrophin and cortisone.

Case 1

A farmer aged 29 developed ulcerative colitis in 1951, and suffered from two severe attacks requiring treatment in hospital before he was seen by us. The present episode

began in October, 1954, with severe diarrhoea and much blood and mucus in the stools. Three weeks later (November 1) he was admitted to the Radcliffe Infirmary with fever, tachycardia, and evidence of considerable loss of weight. He was passing about seven stools a day, which were fluid and composed chiefly of blood with an admixture of liquid faeces, pus, and mucus. Hb, 16.3 g. per 100 ml.; E.S.R., 13 mm. in one hour (Westergren). There was some disturbance of blood chemistry, with a low potassium value (14.2 mg. per 100 ml., or 3.6 mEq per litre). Barium enema showed typical changes of ulcerative colitis extending from the rectum up to the middle of the transverse colon. Sigmoidoscopy revealed an intensely hyperaemic mucous membrane with a granular surface. Passage of the instrument and gentle swabbing with gauze caused free bleeding. A biopsy was taken.

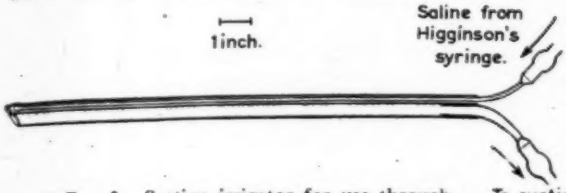


FIG. 3.—Suction irrigator for use through a sigmoidoscope.

Biopsy 1.—The superficial epithelium is rather flattened and darkly staining and there are occasional tiny erosions. One erosion is in relation to a thrombosed subepithelial capillary. The lamina propria is oedematous and infiltrated by lymphocytes, plasma cells, and eosinophil leucocytes. Goblet cells both in the glands and superficial epithelium are reduced in number.

Measures to correct the electrolyte disturbances were successfully adopted, but without effect on the patient's general condition or the bloody diarrhoea. Six days after his admission treatment with cortisone by mouth in a dose of 50 mg. four times a day was begun. Three days later the haemoglobin level having fallen to 10.8 g. per 100 ml., 2 pints (1.1 litres) of whole blood was transfused. Cortisone therapy was continued for two weeks without any appreciable improvement in the patient's condition. At the end of this time he was passing ten stools a day containing much blood and he had lost 10 lb. (4.5 kg.) in weight. Sigmoidoscopy with biopsy was performed after one week and also after two weeks. There was no sigmoidoscopic improvement on the first of these examinations, and there was deterioration on the second in so far as passing the instrument caused the mucosa to bleed even more freely than on earlier examinations.

Biopsy 2.—Inflammatory changes are more intense than in Biopsy 1. In particular, there are larger superficial erosions, and neutrophil granulocytes are more frequent in the cellular exudate. There are small plugs of fibrinous exudate containing polymorphonuclear leucocytes on the surface of some erosions. Congestion of the capillaries and interstitial oedema are marked. In places small pseudo-villous projections of the superficial mucosa can be seen.

Biopsy 3.—The appearances are similar to those in the previous biopsy, but no erosions are seen.

At this stage (November 20) we decided to discontinue cortisone therapy and to give corticotrophin instead in the form of daily intramuscular injections of 100 units of the gel. The response was good. Within four days the daily number of stools had fallen to four and his general condition was improving. Thereafter he made an uninterrupted recovery, and ten days after the introduction of corticotrophin therapy he was passing only one stool a day with a small amount of blood. During this period the only additional therapy was a transfusion of 3 pints (1.7 litres) of blood. He continued to pass one or two normally formed stools a day gradually becoming completely free from blood.

During the phase of clinical improvement on corticotrophin therapy the sigmoidoscopic picture showed undoubted improvement with less vascularity, and there was no bleeding on passing the instrument. A biopsy specimen taken early in this phase still showed gross inflammatory changes.

Biopsy 4 (November 30).—Mucosal inflammatory changes, including capillary congestion, interstitial oedema, and infiltration by plasma cells, lymphocytes, and eosinophil granulocytes, are still present. One glandular tubule shows infiltration with polymorphonuclear leucocytes. There are small patches of subepithelial oedema and occasional tiny superficial erosions.

Two subsequent biopsy specimens during this phase of improvement showed a remarkable change towards normal appearances.

Biopsies 5 and 6 (December 13).—As compared with the previous four biopsies there is a striking change. The superficial and glandular epithelium is essentially normal. Occasional patches of oedema and haemorrhage are present in the interstitial tissue, but the cellular content is not abnormal.

When the patient left hospital on December 23, 1954, he was symptom-free and gaining weight. He continued in clinical remission and the sigmoidoscopic and histological appearances were essentially normal. The corticotrophin was gradually reduced, and finally discontinued on March 12, 1955. He then weighed 12 st. 11 lb. (81.2 kg.) and was in robust health. Three weeks later he was normal in all respects.

A summary of the findings in this case is given in Table I. Biopsies illustrating the three phases of severe symptoms, clinical improvement, and remission are reproduced in the Special Plate.

Case 2

A housewife aged 29 was first admitted to hospital under our care in May, 1954, with a three-year history of passing blood and mucus with her motions and with intermittent diarrhoea in addition. The sigmoidoscopic appearances were

TABLE I.—*Summary of Findings in Case 1*

Biopsy No.	Date	Hormone Therapy	Clinical Picture	Sigmoidoscopy	Histology
1	Nov. 5, 1954	—	Ill with severe bloody diarrhoea	Intensely hyperaemic mucosa, which bled freely	Marked inflammation. Erosion
2	Nov. 13, 1954	Cortisone, 50 mg. q.d.s.	Unchanged	Unchanged	Marked inflammation. Several erosions
3	Nov. 20, 1954	,, ,,	Unchanged. Ten motions a day, chiefly blood	Worse	Marked inflammation
4	Nov. 30, 1954	A.C.T.H. gel, 100 units daily	Greatly improved. One motion a day with small amount of blood	Much improved. Slight hyperaemia and granularity	Inflammation. Erosion
5	Dec. 13, 1954	,, ,,	Still improving. Bowels normal. General condition better	Approaching normal	No inflammation
6	Dec. 23, 1954	,, ,,	General condition greatly improved. Bowels normal	Almost normal	,, ,,
7	Jan. 7, 1955	A.C.T.H., 80 units daily	Well	Normal	,, ,,
8	Feb. 28, 1955	A.C.T.H., 40 units on alternate days	,,	,,	,, ,,
9	Mar. 28, 1955	—	,,	,,	,, ,,

TABLE II.—*Summary of Findings in Case 2*

Biopsy No.	Date	Hormone Therapy	Clinical Picture	Sigmoidoscopy	Histology
1	Nov. 22, 1954	—	General condition good. Passing blood per rectum with each motion	Hyperaemia and granularity of rectal mucosa	Severe inflammation
2	Nov. 29, 1954	Cortisone, 25 mg. q.d.s.	Unchanged	Unchanged	Severe inflammation. Erosions
3	Dec. 16, 1954	,, ,,	Improving. Almost normal	Almost normal	Inflammatory changes less severe. No erosions
4	Jan. 7, 1955	,, ,,	Occasional trace of blood in stools	,, ,,	Slight residual inflammation
5	Feb. 28, 1955	,, ,,	,, ,,	,, ,,	Almost normal
6	Mar. 31, 1955	—	Occasional trace of blood in stools; otherwise normal	,, ,,	Normal

those of mild ulcerative colitis extending up to 20 cm. from the anal margin. She responded rapidly and completely to intramuscular corticotrophin. Thereafter she remained symptom-free until September, 1954, when she again passed blood per rectum. Sigmoidoscopy on October 4 and November 22 showed gross hyperaemia of the mucosa of the rectum and lower sigmoid colon, with bleeding on gentle swabbing.

Biopsy 1 (November 22).—There are marked mucosal inflammatory changes. The superficial epithelium is composed of darkly staining flattened and cuboidal cells and shows occasional foci of degenerate cells and small erosions. The interglandular connective tissue is heavily infiltrated with lymphocytes and plasma cells and contains fairly numerous eosinophil granulocytes and polymorphonuclear leucocytes. Polymorphs are also seen transmigrating the surface epithelium and gland tubules.

At this stage treatment with cortisone in a dose of 25 mg. four times a day by mouth was started. Two weeks later there was no change in her clinical state or in the sigmoidoscopic appearances. A second biopsy showed no improvement.

After a further 18 days of treatment she was almost symptom-free, a small amount of blood being passed only occasionally. Sigmoidoscopy showed only patchy hyperaemia and granularity in the rectum.

Biopsy 3 (December 18).—As compared with the previous biopsies inflammatory changes are much less marked, although increased numbers of lymphocytes, plasma cells, and eosinophil granulocytes are still present.

Treatment was continued and she was kept under observation. She remained feeling well, the only symptom being an occasional trace of blood at the end of defaecation. Sigmoidoscopy on January 7, 1955, showed very slight granularity of the rectal mucosa but no other abnormality, and Biopsy 4 showed further improvement in the histological picture. She continued well apart from the occasional passage of a trace of blood with the motions. The dosage of cortisone was then reduced, and treatment was finally stopped on March 5. On March 31 she remained well.

Biopsy 5 (February 28).—Slight generalized interstitial oedema and increase in lymphocytes.

Biopsy 6 (March 31).—Normal colonic mucosa, with slight interstitial haemorrhage of traumatic origin.

The findings in this case are summarized in Table II, and the histological appearances are illustrated in the Special Plate.

Discussion

Most authors seem to be agreed that the histological changes in ulcerative colitis are those of a non-specific inflammation. The changes found in specimens of the bowel obtained surgically or *post mortem* have been well described by Warren and Sommers (1949); and biopsy studies have been made by Levine and others (1951), including some on patients who were responding favourably to corticotrophin therapy.

In the present paper we describe a method of studying the histology of the mucosa of the bowel in relation to the changes observed in the clinical picture and on sigmoidoscopy throughout the course of treatment with corticotrophin or cortisone. In the two patients studied, biopsy specimens taken when the disease was clinically active showed marked inflammatory changes in the mucosa. Clinical remission was accompanied by sigmoidoscopic improvement and reversion of the mucosa to normal. It would be manifestly unwise to read too much into so small a study, but we consider that further use of the method may improve our knowledge of ulcerative colitis. In particular, the possibility exists that we may find that administration of corticotrophin and cortisone needs to be continued until the mucosa is histologically normal if rapid relapse is not to follow cessation of treatment. Another possibility is that the method will find some application when new treatments require evaluation.

We must emphasize that the method is at present purely a research procedure which is not intended to supplant the conventional methods of colonic biopsy. Colonic biopsy is widely used in the diagnosis of carcinoma and other discrete lesions of the rectum and lower bowel, and an excellent account of the methods available has been given by Gabriel and others (1951). However, these conventional methods involve the removal of a considerably larger fragment of mucosa than we have chosen to work with, and we do not consider that they would be safe methods to use for repeated biopsy studies such as we have made.

From the point of view of the information it can yield, the gravest objection to the present method is that it deals with only a tiny sample of a large stretch of mucous membrane. A similar objection applies to all biopsy methods, such as needle biopsy of the liver, sternal puncture, and gastric biopsy, and accounts for their occasional errors without seriously weakening their great value. In the case of ulcerative colitis the mucosa is diffusely inflamed and the biopsy is carried out under direct vision, so this objection has less weight. Moreover, by taking successive biopsies on a larger group of patients it will soon become clear whether random sampling errors are large enough to nullify the possible uses of the method.

No research method should be used without due attention to its possible risks to the patient. We believe that the risk with our method is slight, although theoretically any break in the rectal or colonic mucosa may predispose to ischiorectal abscess or perforation of the bowel. So far as we have gone, the small erosions created by the biopsy have healed by the next examination, without visible scarring or other evidence of damage. It should also, perhaps, be mentioned that the repeated sigmoidoscopic examinations with biopsy were made with the understanding and willing co-operation of the patients concerned.

Summary

A method of colonic biopsy which is suitable for studying the mucosal changes in ulcerative colitis during the course of the illness is described.

Several biopsy specimens have been taken from each of two patients who responded well to treatment with corticotrophin or cortisone.

The mucosa initially showed marked inflammatory changes. As clinical remission occurred there was

corresponding sigmoidoscopic improvement and the mucosa reverted to normal.

Some possible uses of this method of study are discussed.

REFERENCES

Boston, F. K., and Macintosh, R. R. (1939). *Brit. dent. J.*, **66**, 575.
Gabriel, W. B., Dukes, C. E., and Bussey, H. J. R. (1951). *Brit. J. Surg.*, **38**, 401.
Levine, M. D., Kirsner, J. B., and Klotz, A. P. (1951). *Science*, **114**, 552.
Saher, N. F., and Salt, R. (1943). *British Medical Journal*, **1**, 790.
Truelove, S. C., and Witts, L. J. (1954). Ibid., **2**, 375.
Warren, S., and Sommers, S. C. (1949). *Amer. J. Path.*, **25**, 657.
Wood, I. J., Doig, R. K., Motteram, R., and Hughes, A. (1949). *Lancet*, **1**, 18.

GIANT-CELL ARTERITIS WITH ANEURYSMS

EFFECTS OF HORMONE THERAPY

BY

R. J. HARRISON, M.R.C.P.
Physician, St. James' Hospital, London

C. V. HARRISON, M.D.
Professor of Morbid Anatomy, University of London, Postgraduate Medical School of London

AND

H. KOPELMAN, M.D., M.R.C.P.
Physician, St. Margaret's Hospital, Epping

[WITH SPECIAL PLATE]

Giant-cell or temporal arteritis is now a well-recognized entity with which most physicians and pathologists are familiar. The morphological changes were surveyed by one of us a few years ago (Harrison, 1948), and the clinical picture has recently been reviewed by Roux (1954), who traced over 200 cases in the literature. Our reasons for recording another two cases are: (1) to draw attention to some of the less common manifestations of the disease; and (2) to describe the effects of hormone therapy on the histology of the arterial lesions, our findings in this respect being different from those of previous workers.

Case 1

A 56-year-old housewife was well until December, 1953, when she complained of lassitude, gradual loss of weight, and night sweats. She also had a non-productive cough, for which her practitioner prescribed a linctus and phenobarbitone. In July, 1954, she noticed a painless swelling in the right side of her neck, and a week later a similar swelling appeared in the right infraclavicular region.

At this time there was a pulsating aneurysmal dilatation of the right external carotid artery 1½ in. (3.75 cm.) long and 1 in. (2.5 cm.) across. Similar aneurysmal swellings were also present in the left and right infraclavicular regions and in the right axilla. The fingers of the right hand showed early clubbing, and this hand was warmer than the left. She was afebrile, and weighed 9 st. 12 lb. (62.6 kg.). There was no skin rash or muscle tenderness and no arthritis. Her blood pressure was 130/90 mm. Hg and her pulse 84. No other abnormality was found on clinical examination.

Blood culture was sterile on three occasions. Examination of the blood showed: Hb 75% (Haldane); W.B.C. 11,000 per c.mm. (differential count normal); albumin 3.2 g. and globulin 3.7 g. per 100 ml. (A./G. ratio 0.9); blood urea 19 mg. per 100 ml.; Wassermann reaction negative. Urine: no albumin; centrifuged deposit—no R.B.C. E.S.R. 80 mm. in one hour (Westergren).

Giant-cell arteritis was suspected, and 15 mm. of the affected left suprascapular artery was removed for examination. The specimen contained one small segment of artery that was healthy, the rest being enlarged to twice the normal diameter. Microscopically the lumen in the thickened part of the artery was reduced to a slit by massive thickening of the intima by loose mucoid connective tissue infiltrated with inflammatory cells (Special Plate, Fig. 1). The media was virtually destroyed for about half its circumference, the elastica being broken into fragments. There was a heavy cellular infiltration consisting of polymorphonuclear leucocytes, macrophages, and lymphocytes. Giant cells were seen in relation to fragmented elastic tissue. The picture was typical of giant-cell arteritis in an active stage.

As soon as the diagnosis was confirmed oral administration of cortisone was started, 200 mg. being given daily during the first week. Thereafter the daily dosage was 150 mg. during the second, 100 mg. during the third, 50 mg. during the fourth, and 25 mg. during the fifth week. After the first week the erythrocyte sedimentation rate (E.S.R.) fell to normal and remained so; during and after the course of treatment the patient experienced a general feeling of well-being. No significant change in her weight or blood pressure occurred during treatment.

There was still some doubt whether the inflammatory processes were still active or not, and a second biopsy was performed five weeks after the first, the right acromio-thoracic axis being exposed by a transverse incision below the clavicle. The axis itself was dilated; a large fusiform aneurysm of the axillary artery at least 4 cm. in diameter was defined and palpated. The acromio-thoracic axis with its four branches was removed for section. On microscopical examination the main artery showed signs of healed arteritis (Plate, Fig. 2), but its branches were normal. The intima was thickened by loose mucoid connective tissue exactly like that of the earlier biopsy. For about half the circumference the elastica was fragmented and the media thinned (owing to loss of most of its muscle) and vascularized. In spite of these changes there was no inflammatory cellular infiltration.

For fear of recrudescence an oral maintenance dose of 25 mg. cortisone daily was continued. By December the aneurysmal swelling of the right external carotid artery had disappeared. In early January there was severe pain in the right arm with increased swelling in the right axillary region. This persisted, and after several days the right hand and fingers were numb and cold. On January 17 there was sudden onset of right wrist-drop with loss of sensation over the upper limb and especially marked in the right hand. The swelling in the axilla was no longer pulsatile and was very firm; no bruit was heard over it. The E.S.R. at this time was 11 mm. in one hour (Westergren). It was considered that there was a large thrombosed aneurysm in the axilla, and this was confirmed by arteriography. An operation to relieve nerve pressure was performed on January 25, cortisone treatment being discontinued.

At operation (Mr. Andrew M. Desmond) the main mass of the aneurysm was found to be false and occupying the lower part of the axilla. The smaller upper part of the aneurysm was a fusiform dilatation apparently of the subclavian artery just beyond the acromio-thoracic axis. There was no demonstrable communication between the two parts of the aneurysm. The false aneurysm was opened, the clot evacuated, and the bleeding controlled. A piece of the end of the aneurysm and the adjoining vessel was taken for histological examination.

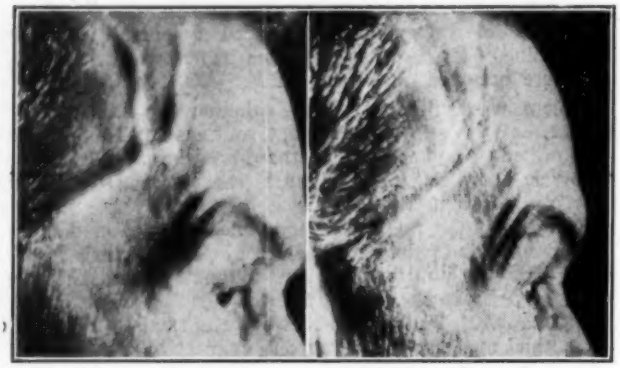
Sections from the normal part of the vessel disclosed that it was a vein and not an artery as supposed. At this level the intima showed some thickening and there were a few minute foci of cellular infiltration in the intima and media; in other respects the part was healthy. A longitudinal section through the end of the aneurysm (Plate, Fig. 3) showed thinning-out of the vein wall without (in the tissue taken) any sign of medial destruction. An organizing thrombus was attached to one wall close to a venous valve; there was no sign of inflammatory activity. Fragments from the wall of the false aneurysm showed only fibrous tissue with no vascular residue.

Since the operation the patient has had physiotherapy daily, and there has been a fair degree of recovery of function of the right arm and hand. On March 30 the E.S.R. was 5 mm. in one hour.

The cortisone used for this case was supplied by the Medical Research Council for clinical trial.

Case 2

A retired policeman aged 76 was admitted on March 16, 1953, with severe throbbing headaches in the temporal regions extending to the top of the cranium, the angles of the jaw, and the neck. Although there had been slight improvement, the pain was severe and not relieved by the usual analgesics. Both temporal arteries appeared to be greatly thickened (Fig. A) and were extremely tender to palpation. Apart from this he was very fit for his age; his blood pressure was 170/90 mm. Hg, the fundi were normal, and there was no leucocytosis. His E.S.R. was 36 mm. in one hour.



A B

Case 2. Showing right temporal artery (A) before treatment, and (B) after treatment and immediately before second biopsy was taken.

On March 23 a biopsy and ligation of the left temporal artery was performed under local analgesia. The next day pain in the left temporal artery was much less and there was slight improvement on the opposite side, but by the 25th the pain had returned in the ligated artery proximal to the ligation. The distal part of the artery was, however, much less tender to palpation. The opposite artery remained unchanged. On the 27th A.C.T.H. gel was given by injection, 25 mg. three times a day. Within 24 hours the pain was completely relieved, and after 48 hours the artery became much less thickened, pulsatile, and no longer tender (Fig. B).

After eleven days' treatment a biopsy taken from the second artery showed the process to be inactive, and it was felt safe to reduce the dose of A.C.T.H. slowly over a period of seven days and finally to omit it. The patient has remained well and symptom-free since.

At the first biopsy the histology was typical of giant-cell arteritis (Plate, Fig. 4). The lumen of the artery was a minute slit. The inner half of the intima was composed of active fibroblastic connective tissue, and the outer half was invaded by vasa infiltrated by polymorphonuclear leucocytes and macrophages with a few eosinophil granulocytes and plasma cells. The internal elastic lamina was fragmented and there were giant cells among the fragments. The media was infiltrated by cells like those in the intima. The adventitia was thickened and infiltrated by a few cells, mostly plasma cells.

The histological appearances of the specimen taken after treatment were totally different (Plate, Fig. 5). The artery was almost exactly half the diameter of the earlier one. As before, the lumen was reduced to a slit and there was the same degree of intimal thickening, but there was now no cellular infiltration. The internal elastic lamina was fragmented but no longer the site of a giant-cell reaction. The media similarly had completely lost its cellular infiltration, though in places it was still traversed by enlarged vasa. Finally, the adventitia was of about normal thickness, and the only sign of previous involvement was the presence of a few groups of lymphocytes.

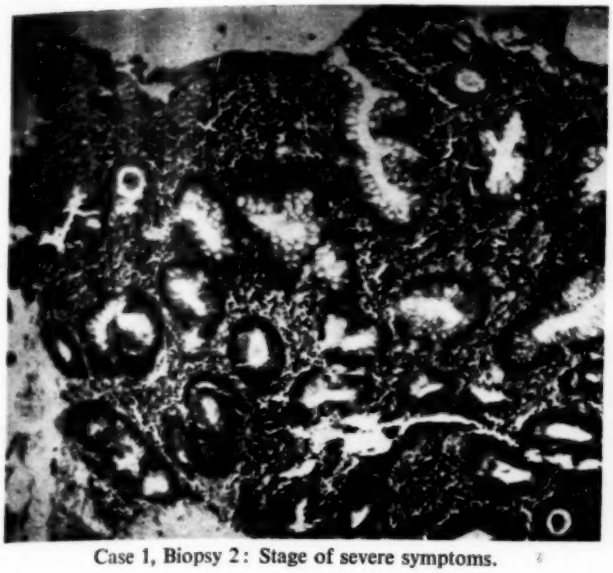
Discussion

The first case showed a number of unusual features: although for some months the patient had had lassitude, night sweats, and loss of weight, she did not suffer from headaches or from pain in any of the affected regions. The occurrence of saccular aneurysms is even more unusual. We have been able to trace only two other cases: the first was Gilmour's (1941) Case I, in which the patient died of a ruptured subclavian aneurysm, and the other the remarkable case of Gelfand (1955) of an aortic and a subclavian aneurysm in an African boy of 2 years. In addition to these two cases, Magarey (1950) described a fatal dissecting aneurysm of the aorta, and McMillan (1950) a partial aortic tear without dissection. Aneurysms occur rarely in a disease which causes such severe medial damage as giant-cell arteritis; when they do they appear to affect only the larger vessels, and we would like to suggest a possible explanation for this. The stress in the wall of an artery is related not only to the pressure within, but also to the size of the lumen. In small arteries the lumen is rapidly reduced by the intimal overgrowth that is such a characteristic feature of this disease. In larger arteries like the subclavian, on the other hand, even a considerable degree of intimal thickening will not reduce the lumen sufficiently to protect a damaged media.

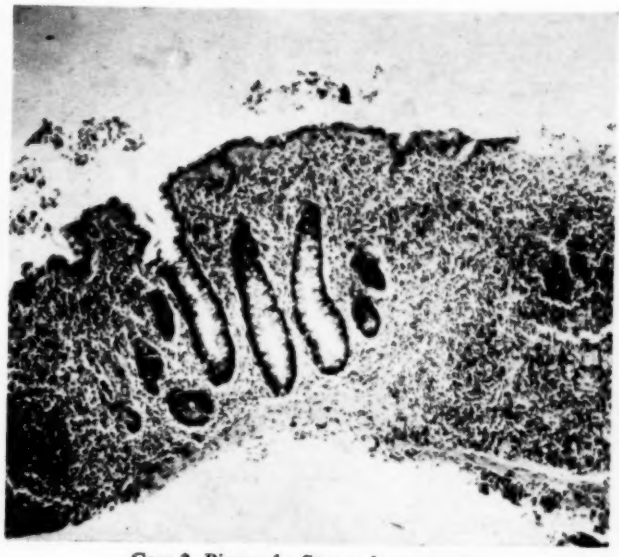
The use of either cortisone or A.C.T.H. is now well established in the treatment of this disease (Roux, 1954). Usually there has been prompt and dramatic relief of symptoms and slower improvement of physical signs, but the effect is suppressive and the disease is apt to flame up if treatment is not continued long enough. Occasionally treatment fails, and Fabian (1952) records a case confirmed by biopsy in which there was no clinical improvement. The effect of hormone treatment on the structural changes in the vessels is less certain, because only a few cases have been subjected to biopsy before and after treatment. We have found reports of four such cases. Siegert (1952) gave an injection of depot cortisone and took a second biopsy after 12 days. Höok and Jernelius (1952) gave 1 g. of cortisone over a period of a month. Oösthuizen and Van Wyk (1954) 20 mg. of A.C.T.H. four-hourly for 12 days, and Roux (1954) 13 g. of cortisone over 12 days, before taking a second biopsy. In all four cases the authors report clinical improvement, but in no case was there any significant change in histological appearance.

In both our own cases there was striking regression of the inflammatory reaction, and in fact we believe that they are the first cases reported in which serial biopsy has shown such structural change. We are unable to offer any satisfactory explanation. It might be argued that in the second biopsies the arteries had not been affected or had undergone spontaneous healing before treatment. The former argument seems to be disproved by the clinical change and the severe scarring that was present, and the second by the obvious clinical change that had taken place in an easily palpable artery. The dose of hormone used might be thought to explain the difference; our first case certainly received a much greater dose of cortisone than other published cases. In our second case, however, the dose of A.C.T.H. was less than that given, for example, by Oösthuizen and Van Wyk.

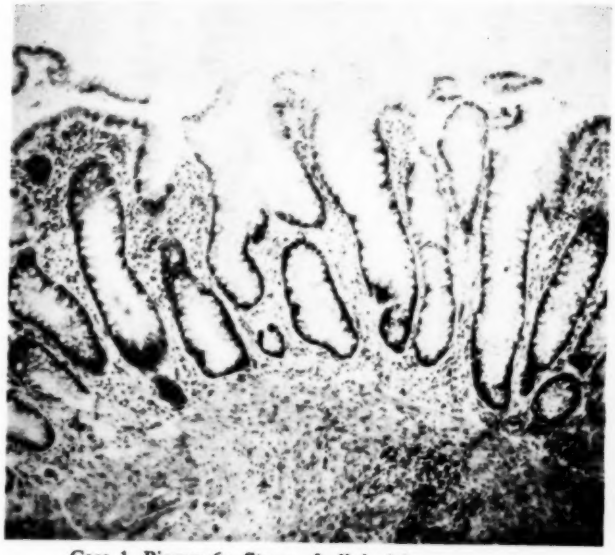
The clinical and histological evidence that we have is that cortisone and A.C.T.H. reduce the oedema and the inflammatory cellular reactions. This is probably the cause of the relief of symptoms. There is no evidence that the treatment has any effect on the scarring and intimal thickening that has already taken place; in fact in the first case thrombosis occurred despite treatment. It seems probable



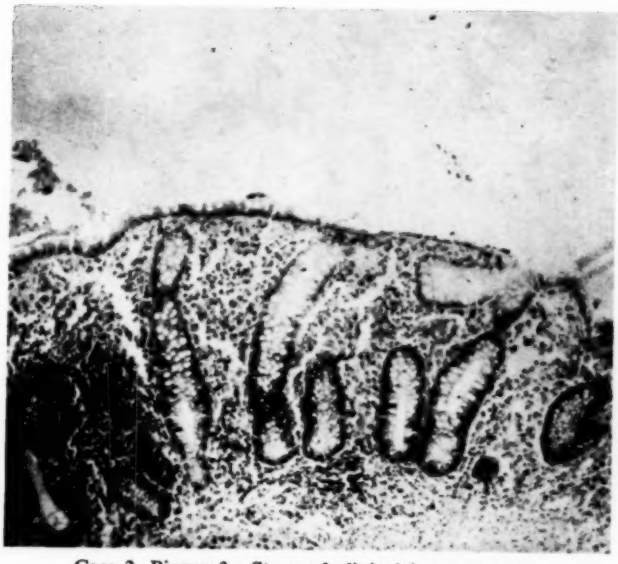
Case 1, Biopsy 2: Stage of severe symptoms.



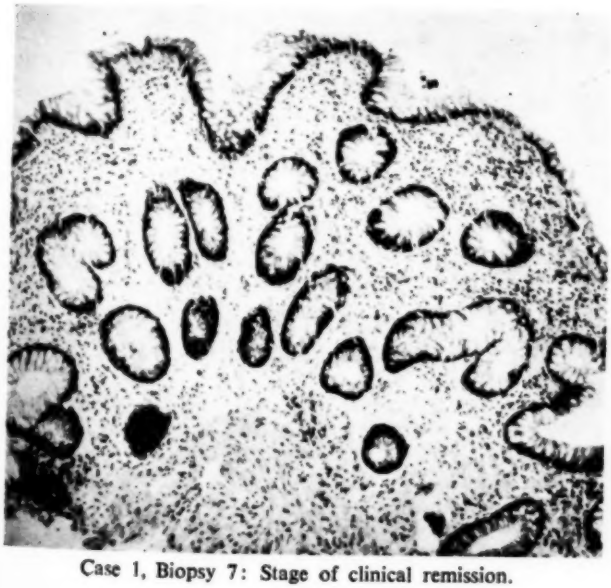
Case 2, Biopsy 1: Stage of symptoms.



Case 1, Biopsy 6: Stage of clinical improvement.

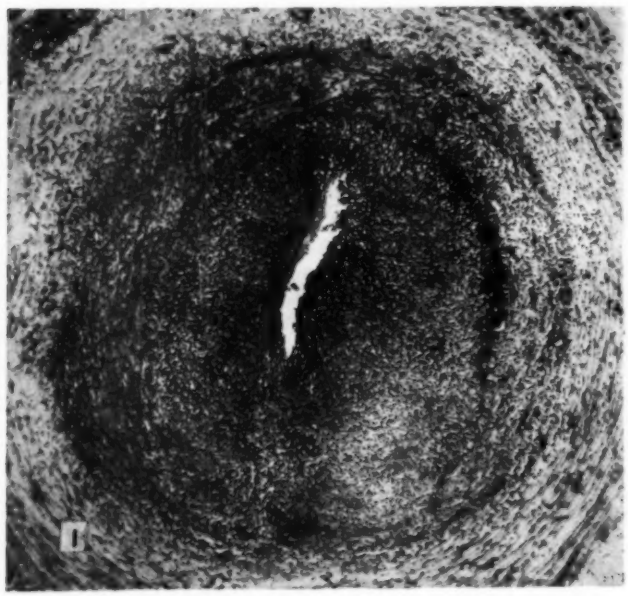


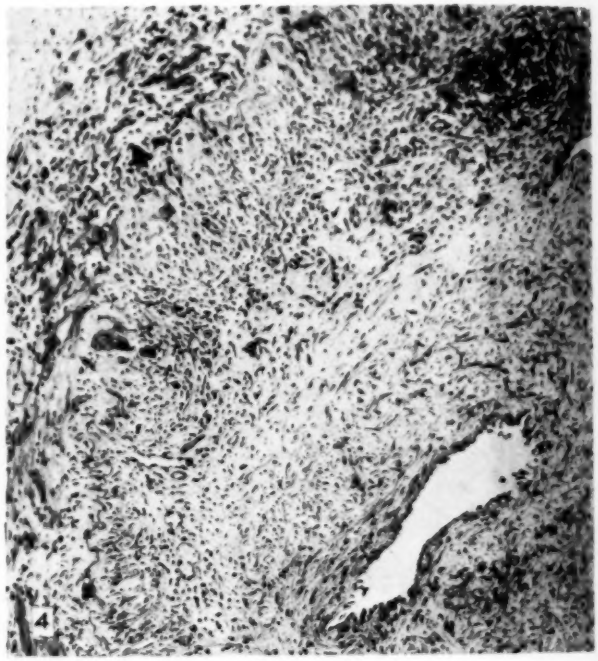
Case 2, Biopsy 3: Stage of clinical improvement.



Case 1, Biopsy 7: Stage of clinical remission.

Case 2, Biopsy 6: Stage of clinical remission.





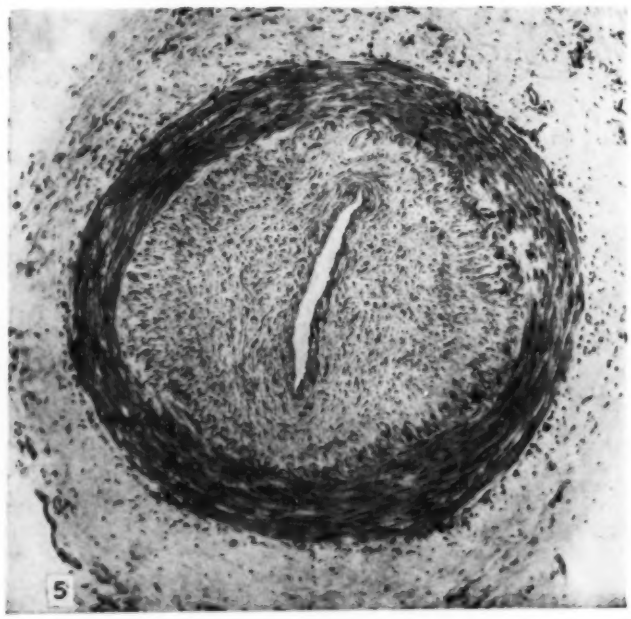


FIG. 1.—Case 1: Left suprascapular artery before treatment. The intima is greatly thickened, leaving a slit-like lumen. The media is destroyed in the lower two-thirds and both coats are heavily infiltrated with inflammatory cells. (Haematoxylin and eosin. ×30.)

FIG. 2.—Case 1: Acromio-thoracic axis after treatment. Intimal thickening unchanged. Media interrupted by fibrous scars, but both coats free from cellular infiltration. (The black crescent is operative haemorrhage in the vessel wall.) (Haematoxylin and eosin. ×30.)

FIG. 3.—Case 1: Subclavian vein showing aneurysm. A mass of thrombus is present to the left of the valve. (Haematoxylin and eosin. ×19.)

FIG. 4.—Case 2: Left temporal artery before treatment, showing intimal thickening and heavy cellular infiltration including giant cells. (Haematoxylin and eosin. ×73.)

FIG. 5.—Case 2: Right temporal artery after treatment. The intimal thickening is unaltered, but the artery has returned to normal size and is totally free from cellular infiltration. Fragmentation of elastic tissue not visible in this section. (Haematoxylin and eosin. ×73.)

R. FINLAYSON AND J. O. ROBINSON: GIANT-CELL ARTERITIS OF LEGS

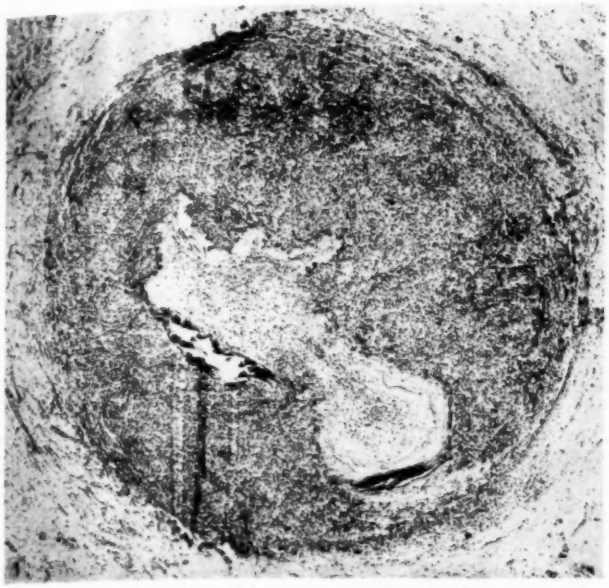


FIG. 1.—Left posterior tibial artery: occlusion of lumen by connective tissue containing moderate numbers of cells, with diffuse cellular infiltration of media. (Haematoxylin and eosin. ×24.5.)

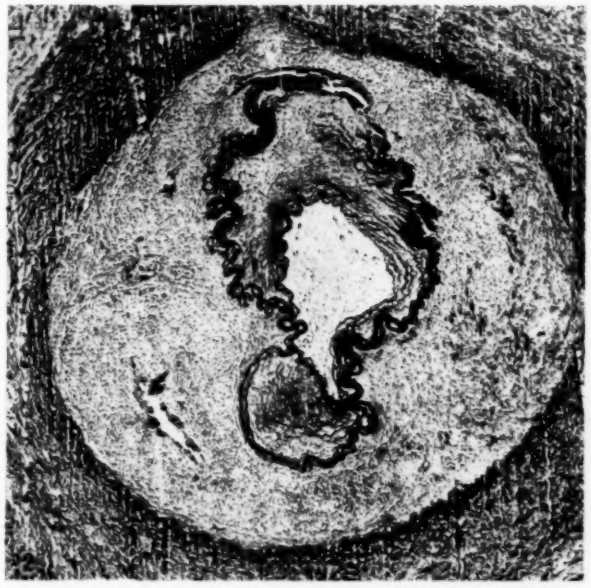
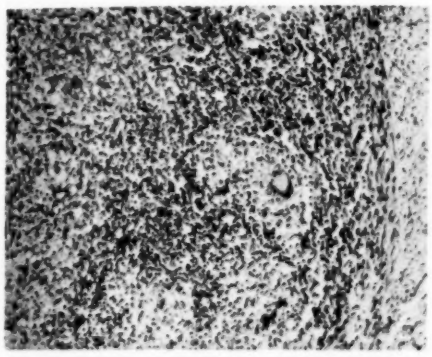


FIG. 2.—Left anterior tibial artery: proliferation, splitting, and bulging of internal elastic lamina. Small segmental deficiency of lamina adjacent to calcified medial plaque. (Weigert-van Gieson. ×28.)



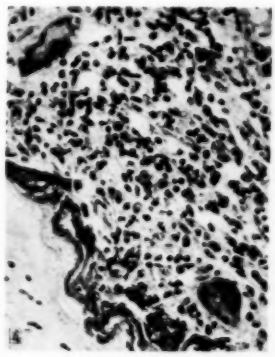


FIG. 3.—Part of wall of left anterior tibial artery: intense chronic inflammatory cellular infiltration of media, with foci simulating tuberculous follicles. Smooth-muscle cells clearly identified only by adventitia on right. (H. & E. ×75.)

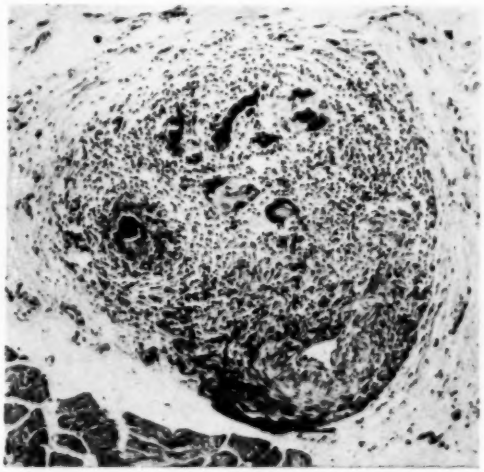


FIG. 4.—Left posterior tibial artery: infiltration of media with giant cells, lymphocytes, plasma cells, and histiocytes. Irregular staining of internal elastic lamina with calcification. (Haematoxylin and eosin. ×165.)

FIG. 5.—Small artery from right tibialis anterior muscle: focal infiltration of media, adventitia, and perivascular connective tissue with lymphocytes and giant cells, the latter related in part to small areas of calcification. (Haematoxylin and eosin. ×80.)

P. F. MILNER: NASAL GRANULOMA AND PERIARTERITIS NODOSA

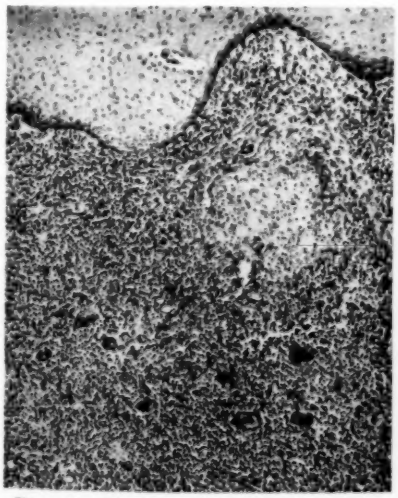


FIG. 1.—Biopsy of gingival tumour showing multinucleate giant cells in the dermis. (Haematoxylin and eosin. ×60.)

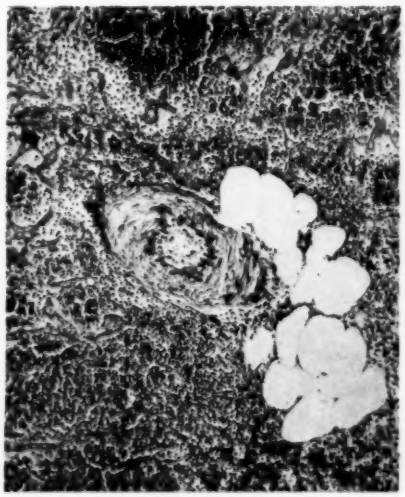


FIG. 2.—Skin over right deltoid: normal vessel in subcutaneous fat surrounded by organizing haemorrhage. (H. & E. ×65.)

FIG. 3.—Kidney, showing hyaline necrosis and fibrosis of glomeruli with oedema and inflammatory exudate. (H. & E. ×60.)

G. A. GRANT PETERKIN: ERYTHEMA AB IGNE

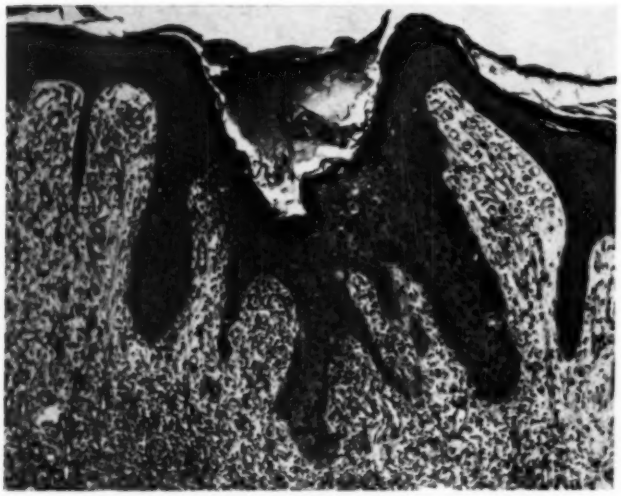


FIG. 1.—Case 4: Photomicrograph (×68) from nodular lesion on left leg.

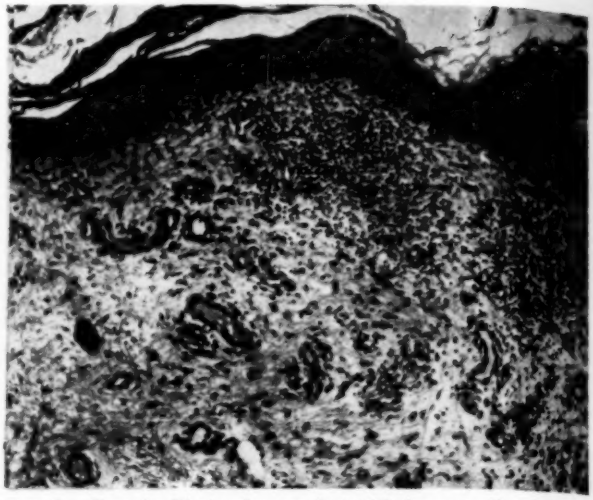


FIG. 2.—Case 4: Photomicrograph (×68) from small nodule on right leg.

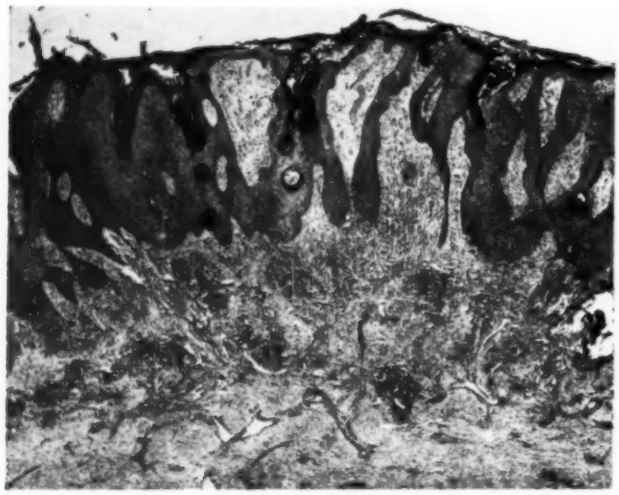


FIG. 3.—Case 4: Photomicrograph (×15) of section from large nodule on left leg, showing squamous-cell carcinoma.

FIG. 4.—Case 4: Photomicrograph (×68) of squamous-cell carcinoma.

J. D. GRIFFITHS AND D. F. ELLISON NASH: PNEUMATOSIS CYSTOIDES INTESTINALIS

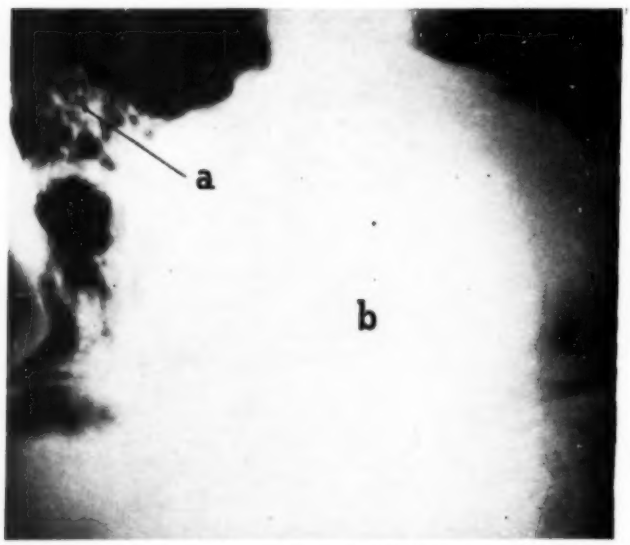


FIG. 1.—Antero-posterior radiograph of abdomen. (*a*) Loculated gas beneath right dome of diaphragm. (*b*) Complete obscuring of central abdominal area by stomach grossly distended with blood clot.

FIG. 2.—Photograph of specimen of resected small intestine showing on left relatively collapsed segment with submucosal cysts, and on right (top) the opened proximal portion containing large intramural cysts. The intervening mass consisted of strictured bowel and contracted mesentery packed with large and small cysts.

that it is thrombus which causes the arterial obstruction and symptoms after cortisone has been given, and it might be argued that there is an indication for the use of anticoagulants during and following cortisone therapy.

Summary

Two cases of giant-cell arteritis—one with the formation of saccular aneurysms—in a woman of 56 and a man of 76 are presented. Treatment was respectively with cortisone orally and A.C.T.H. by injection. Both patients recovered. The histological findings both before and after treatment are described and illustrated. A possible explanation of why aneurysms occur only in the larger vessels in giant-cell arteritis is offered. The advantages of a second biopsy after completion of treatment, with a view to assessing the degree of structural recovery, are pointed out.

REFERENCES

Fabian, G. (1952). *Klin. Mbl. Augenheilk.*, **121**, 80.
Gelfand, M. (1955). *Brit. Heart J.*, **17**, 264.
Gilmour, J. R. (1941). *J. Path. Bact.*, **53**, 263.
Harrison, C. V. (1948). *J. clin. Path.*, **1**, 197.
Höok, O., and Jernelius, B. (1952). *Nord. Med.*, **48**, 1224.
McMillan, G. C. (1950). *Arch. Path. (Chicago)*, **49**, 63.
Magarey, F. R. (1950). *J. Path. Bact.*, **62**, 445.
Oösthuizen, W. J., and Van Wyk, F. A. K. (1954). *S. Afr. med. J.*, **28**, 310.
Roux, J. L. (1954). *Helv. med. Acta*, **21**, Suppl. 34.
Siegert, P. (1952). *Klin. Mbl. Augenheilk.*, **120**, 254.

GIANT-CELL ARTERITIS OF THE LEGS

BY

R. FINLAYSON, M.B., B.Chir.

AND

J. O. ROBINSON, M.Chir., F.R.C.S.

From the Departments of Pathology and Surgery, St. Bartholomew's Hospital, London

[WITH SPECIAL PLATE]

Giant-cell or temporal arteritis was described clinically by Hutchinson in 1890, but it was not until 1934 that Horton *et al.* recognized the histological features. The condition was initially believed to be localized to the temporal arteries, but of recent years it has become apparent that it may be a generalized arterial disease. Visual disturbances and cerebral symptoms are frequent complications, but the development of gangrene in the limbs has rarely been mentioned, and it is for this reason that the following case is thought to be worth recording.

Case Report

A woman aged 75 was admitted to St. Bartholomew's Hospital on July 14, 1954, complaining of pain in both feet. She had suffered with cold feet and chilblains for many years, but these had caused her no serious inconvenience until three months before admission, when she developed a sudden severe pain in both legs, the left leg being the more painful. The legs became white, and were swollen to a level above her knees. A diagnosis of "thrombosis" was made, and after twelve days' confinement to bed the pain and swelling subsided and the colour returned to normal. When she became ambulant she noticed that her feet were colder than before, and that they were blue and stiff. The feet and legs became increasingly painful, but she persisted with her daily housework until two weeks before admission. Following the "thrombosis" she noted that her general health had deteriorated; she had felt a little feverish towards the evening, her appetite had gradually worsened, and tiredness had become a prominent feature.

She was a pale woman with bilateral cataracts. The fundi showed choroidal pigmentation, the veins were normal, but the arteries were sclerosed. There was no evidence of temporal arteritis. Her heart was clinically not enlarged. Her arms were normal. B.P. 140/70; T. 99° F. (37.2° C.); P. 80; R. 22.

Legs.—Left: The foot was swollen and the skin waxen in appearance. The distal half of the foot was cold and dark blue, with patches of white on the toes. The remainder of the foot and limb was warm and of a normal colour. *Right:* The distal third of the foot was cold and dark blue apart from the toes, which were white; the remainder of the foot and limb was warm and of a normal colour; the femoral and popliteal pulses were present in both legs, but pulsation could not be felt in either foot.

Investigations.—Hb, 10.4 g. per 100 ml.; W.B.C., 16,000 per c.mm.; E.S.R., 25 mm. in one hour (Westergren); serum proteins, 6.7 g. per 100 ml. (albumin 3.9 g., globulin 2.8 g.); blood urea, 34 mg. per 100 ml. Urine: No albumin or sugar detected; a centrifuged deposit showed an occasional white blood cell, a few epithelial cells, and red blood corpuscles (one to two in an occasional 1/6 field). Wassermann and Kahn reactions were negative.

X-ray Examination.—Chest film: slight ventricular hypertrophy; lung fields clear. Intravenous pyelogram: both kidneys functioned promptly, with a good concentration. Leg films: there was evidence of a minor degree of vascular calcification.

Operation.—A below-knee amputation of the left leg was performed with a right lumbar sympathectomy on July 16.

Pathological Examination of Left Leg

Except for peripheral gangrene, the only pathological changes noted on dissection of the limb were in the larger arteries, which resembled firm cords. Atheromatous plaques were not evident on macroscopical examination, but the vessel walls showed multiple minute foci of calcification. The accompanying venae comitantes were small, but the vessels were fully patent except for a little recent blood clot in a small lateral plantar vein. The long and short saphenous veins were normal.

Microscopical examination of the anterior tibial, posterior tibial, and peroneal arteries showed essentially similar histological changes. The lumen was either completely obliterated or reduced to a narrow chink by thickening of the intima, resulting from a proliferation of loose, fairly vascular mesenchymal tissue infiltrated with small numbers of chronic inflammatory cells, predominantly lymphocytic in type (Special Plate, Fig. 1). Small foci of atheromatous fatty change were also present in some sections. The internal elastic lamina of the vessels was reduplicated and stained irregularly; the inner fibres, in general, stained indifferently, while the outer fibres appeared highly refractile, and in many areas were closely related to fine or heavy deposits of calcium. The elastica showed some fragmentation, but complete loss of a segment of the internal elastic lamina was seen in two sections only, and at both sites the deficiency was anatomically related to a calcified plaque in the adjacent inner media (Plate, Fig. 2).

There was an intense diffuse cellular infiltration of the media composed mainly of lymphocytes, but also including moderate numbers of histiocytes together with varying numbers of multinucleated giant cells, many with peripherally arranged nuclei, and showing, in some fields, a focal arrangement simulating tuberculous follicles (Plate, Fig. 3). Small to moderate numbers of plasma cells were also identified (Plate, Fig. 4), but neutrophil and eosinophil leucocytes either were absent or were present in very small numbers. The media showed increased vascularity, fibro-

blastic proliferation, multiple foci of calcification, together with vacuolation and some eosinophilic granular debris which was probably derived from degenerate and necrotic smooth muscle cells. In general, normal muscle cells were present only as a thin, irregular peripheral zone adjacent to the adventitia (Plate, Fig. 3). The latter showed fragmentation and destruction of the external elastic lamina with increased fibrosis and slight or minimal lymphocytic cellular infiltration. Ziehl–Neelsen stained sections were negative for acid-fast bacilli. The accompanying venae comitantes showed only slight subintimal thickening and medial fibrosis with no evidence of thrombosis or phlebitis.

The dorsalis pedis artery showed changes similar to those seen in the large arteries except that the narrowed lumen was occluded by a small recent thrombus and that the media of the vessel appeared normal except for some calcification and slight cellular infiltration with lymphocytes and histiocytes. The medial and lateral plantar arteries showed only slight intimal thickening with proliferation of the elastica and slight medial fibrosis. A small lateral plantar vein contained recent thrombus; the other veins showed no significant histological changes. Sections of the smaller vessels of the foot (arcuate, dorsal metatarsals, plantar metatarsals, and digitals), together with adjacent soft tissues, showed widespread acute inflammatory changes. Microscopical examination of the tibialis anterior muscle showed no abnormality. A section of the soleus muscle included a small artery which showed intimal thickening with fairly extensive chronic inflammatory cellular infiltration of the media and adventitia, including small numbers of multinucleated giant cells.

The lesions in the larger arteries of the amputated limb were considered to be those of giant-cell (temporal) arteritis, and a diagnosis of giant-cell arteritis complicated by gangrene of the foot was made. The medial calcification and relatively slight atheromatous changes were regarded as incidental, additional findings. The acute inflammatory changes in the smaller pedal vessels appeared to be non-specific in nature and almost certainly secondary to the gangrenous process.

After the operation the right leg became painless and warmer, and the colour improved. A course of Buerger's exercises was started on the right leg, but on the fourth post-operative day obvious gangrene of the big toe, with oedema and discoloration of the foot, had occurred.

Cortisone was started, but only 150 mg. had been given when it was apparent that surgery must be undertaken to prevent spread of the gangrene.

Operation.—A below-knee amputation of the right leg was performed on July 30.

After each of the amputations a transfusion of 1 pint (570 ml.) of whole blood was given. Recovery from these operations was satisfactory and uneventful. Both stumps healed by first intention and were free of pain. On discharge from hospital she was extremely well; her appetite had returned to normal and she was apyrexial. She was seen again in November on her way to Queen Mary's Hospital, Roehampton, where she was to be fitted with bilateral prostheses. Her general health had remained good and the stumps showed no sign of ischaemia. The E.S.R. had fallen to 9 mm. in one hour (Westergren).

Pathological Examination of Right Leg

Dissection of the anterior tibial, posterior tibial, and peroneal vessels showed changes similar to those observed in the previously amputated left leg. The small arteries of the foot also appeared abnormally thick-walled and stenosed. The firm, cord-like arteries showed little macroscopical evidence of atherosclerosis or of extensive calcification. The distal segment of the anterior tibial artery contained a small central plug of red thrombus. The accompanying venae comitantes were small, but fully patent.

Microscopical examination of the anterior tibial, posterior tibial, and peroneal arteries showed pathological changes similar to those seen in the corresponding vessels of the left leg. The accompanying venae comitantes were essentially normal except that one section of an anterior tibial vein showed a small, cellular intramural focus composed of lymphocytes and small numbers of histiocytes.

Microscopical examination confirmed that the arteritis also involved the dorsalis pedis, medial plantar, and arcuate arteries, all of which showed gross intimal thickening with extensive lympho-histiocytic cellular infiltration and associated muscle-cell degeneration of the media. Sections of the medial plantar artery also showed moderate calcification and giant-cell infiltration of the media. The lateral plantar artery and two dorsal metatarsal arteries showed minimal specific inflammatory changes, and the one plantar metatarsal artery sectioned had a normal media with only slight intimal proliferation. Acute inflammatory changes seen in the walls of the digital vessels were similar to those observed in the left foot and were likewise considered to be non-specific and to be related to the peripheral gangrene.

Serial sections of a block taken from the tibialis anterior muscle included three small arteries showing focal lympho-histiocytic cellular infiltration of the media, adventitia, and perivascular connective tissue with, in one vessel, calcification and associated giant-cell reaction (Special Plate, Fig. 5); other small vessels included in the section appeared normal. Section of one of the long flexor muscles showed occasional small focal collections of lymphocytes situated in the interstitial tissue between the muscle fibres, but the few small vessels included in the section were normal.

Discussion

The clinical findings of fever, anorexia, anaemia, and arterial disease in this case are consistent with a diagnosis of giant-cell arteritis, which is further established by the almost pathognomonic histological changes in the affected arteries. Comparison of the vascular lesions in the two limbs showed a close similarity in the histological changes with only a slight difference in anatomical distribution. Both limbs showed extensive involvement of tibial and peroneal arteries, and while the arteritis in the left leg appeared to fade peripherally at the level of the dorsalis pedis it had extended, on the right side, into the plantar and arcuate vessels. Involvement of small muscle arteries was noted in both specimens, and it is possible that muscle biopsy has a place in the diagnosis of giant-cell arteritis if biopsy of a large artery is contraindicated.

The interesting features of this case are, firstly, the atypical clinical presentation of the disease with its complete absence of symptoms referable to arteritis of any of the cranial vessels and its apparent localization to the arteries of the lower limbs, and, secondly, that the vascular changes were complicated by the development of peripheral gangrene.

Harrison (1947–8) has emphasized the ophthalmic and cerebral complications of this condition, but states that it is certainly significant that, in a disease which causes gross vascular narrowing and affects medium-sized arteries, there is no ischaemic gangrene of the limbs. Harrison refers to one of the cases of temporal arteritis described by Robertson (1947) which developed gangrene of a toe, necessitating amputation. The gangrene was thought to be due to obliterative arteriosclerosis and not to giant-cell arteritis, but the blood vessels in the amputation specimen were not examined histologically. Only two of the 75 cases reviewed by Harrison (1947–8) showed histological evidence of femoral arteritis, and in one other case there was clinical evidence of involvement of a dorsalis pedis artery. Cardell and Hanley (1951) reviewed 27 reported cases of giant-cell arteritis in which necropsy had been performed, and, although the series emphasized the diffuse nature of the vascular lesion, none of the cases had developed peripheral gangrene, and extensive involvement of limb vessels was not recorded. It is, however, impossible

to assess the true extent of the vascular lesions from many of these case reports as post-mortem examination was frequently incomplete.

More recently, Heptinstall *et al.* (1954) have reported 14 cases of giant-cell arteritis, three of which came to necropsy. Vascular changes were widespread in the three fatal cases, and included histologically confirmed lesions in the right femoral artery and left popliteal artery in one case, and in the right popliteal artery in a second case. Pains in the limbs and joints were noted in 5 of the 14 cases—the authors suggested the possibility that the limb pains may be due to specific changes in the arteries—but peripheral gangrene was not encountered. Reference, however, is made to a case reported by Frangenheim (1951) in which a 72-year-old man had suddenly become blind and in which amputation of a leg for gangrene revealed the changes of giant-cell arteritis in the femoral artery. Reference is also made to a case described by Atlas (1943) in which a 68-year-old woman had a leg amputated for gangrene. The case was recorded as one of Buerger's disease, but we agree with Heptinstall *et al.* (1954) that the histological findings are consistent with giant-cell arteritis. In this case the patient died shortly after operation, but whether a necropsy was performed is not recorded.

It is thus apparent that giant-cell arteritis can involve the arteries of the lower limbs and in rare instances be complicated by gangrene. Giant-cell arteritis is a disease of the middle-aged and elderly, and it is therefore very probable that affected limb arteries will also show some degree of incidental atherosclerosis; but unless the latter is extensive it is reasonable to suggest that ischaemic symptoms which may develop are due mainly to the obliterative arteritis which is a well-recognized feature of giant-cell arteritis.

Giant-cell arteritis should therefore be considered in the differential diagnosis of any unexplained case of peripheral vascular disease occurring in the middle-aged or elderly, and if such a diagnosis is substantiated corticotrophin or cortisone therapy should be given before gangrene supervenes and surgery becomes imperative.

Summary

A case of giant-cell arteritis apparently localized to the arteries of the lower limbs and producing gangrene is reported. Both legs had to be amputated, and histological examination showed the typical features of giant-cell arteritis in the tibial and peroneal arteries. One limb also showed involvement of the pedal arteries, and essentially similar changes were noted in some of the small arteries supplying voluntary muscles.

A review of the literature indicates that peripheral gangrene is a rare complication of giant-cell arteritis, but the real incidence of involvement of the leg arteries in this disease is not known. The apparent rarity of this condition may account for its being overlooked in other cases, and it is suggested that giant-cell arteritis should be considered in the differential diagnosis of any unexplained case of peripheral vascular disease occurring in the middle-aged or elderly.

We are indebted to Mr. E. G. Tuckwell for permission to publish this case and to Professor J. W. S. Blacklock for his help and advice. We thank Mr. K. W. Iles for the photomicrographs and Miss Audrey Dixon for the cutting and staining of many sections.

REFERENCES

Atlas, L. N. (1943). *Amer. Heart J.*, **26**, 120.
Cardell, B. S., and Hanley, T. (1951). *J. Path. Bact.*, **63**, 587.
Frangenheim, H. (1951). *Zbl. allg. Path. path. Anat.*, **88**, 81.
Harrison, C. V. (1947-8). *J. clin. Path.*, **1**, 197.
Heptinstall, R. H., Porter, K. A., and Barkley, H. (1954). *J. Path. Bact.*, **67**, 507.
Horton, B. T., Magath, T. B., and Brown, G. E. (1934). *Arch. intern. Med.*, **53**, 400.
Hutchinson, J. (1890). *Arch. Surg. (Lond.)*, **1**, 323.
Robertson, K. (1947). *British Medical Journal*, **2**, 168.

NASAL GRANULOMA AND PERIARTERITIS NODOSA

REPORT OF A CASE

BY

PAUL F. MILNER, M.B., B.Ch.
Captain, R.A.M.C.; formerly Resident in Pathology, Northampton General Hospital

[WITH SPECIAL PLATE]

Since Kussmaul and Maier (1866) gave the name "periarteritis nodosa" to a disease which they were the first to describe, many cases differing in certain clinical and pathological details have been reported. In 1903 Veszprémi and Jancsó made the diagnosis from histological material in a case presenting no gross evidence of the disease; and Mönckeburg (1905) for the first time described lesions of periarteritis in the lungs. The second case with pulmonary-artery involvement, reported by Ophüls (1923), had many distinguishing features, among them granulomatous lesions in serous membranes. Gradually it came to be appreciated that the microscopic form of the disease, affecting small arteries and veins, was the commoner and could be distinguished from the classical disease (Zeek *et al.*, 1948; Zeek, 1952).

Cases of periarteritis nodosa with granulomatous lesions in the upper respiratory tract are uncommon. Godman and Churg (1954), who reported seven cases of their own, were able to find 22 cases in the world literature. Of these, one reported by Howells and Friedmann (1950) and two reported by Stratton *et al.* (1953) are the only British cases in their list. Klinger (1931) was the first to describe a syndrome of severe destructive sinusitis, nephritis, and uraemia. Wegener (1936, 1939), describing three cases of ulcerative granulomata in the upper respiratory tract with periarteritis nodosa, wrote: "The point of origin of the disease was the inner nose, where a putrid, necrotic inflammation was found with granulation tissue and nodular granulomata. This evidently led to sensitization of the body as a whole, resulting in allergic, hyperergic reactions, especially in the vascular system." Stratton *et al.* (1953) stressed that "the essence of this syndrome is that the upper respiratory tract lesions are the first and, at the onset, the dominating feature of the condition." Pulmonary lesions, both vascular and granulomatous, are almost a constant feature of this syndrome; in only one case of the series reviewed by Godman and Churg were they absent. In this case, reported by Lindsay *et al.* (1944), there was a progressive destructive nasal lesion for a year before acute fatal periarteritis nodosa developed.

The case now reported appears unique in two respects: (1) the acute nasal and gingival giant-cell granulomatous lesions regressed and healed before the fatal illness; and (2) no vascular or granulomatous lesions could be found in the lungs at necropsy.

Case Report

A 41-year-old housewife had an upper right premolar extracted in May, 1954. The socket healed well till about June 17, when a bright-red swelling appeared on the gum, which became painful. Two lower left molars were extracted at this time, the sockets failing to heal and becoming swollen and painful. The face then began to swell and she had headaches and nasal discharge. She felt weak

and lethargic, but had not lost weight and had no cough or other symptoms. Until her present illness her general health had always been good.

On admission to an E.N.T. ward on June 26 she had a sessile, bluish-grey, nodular soft swelling of the gum behind the upper right canine. A similar swelling was seen in the $\overline{123}$ region. There was severe oral sepsis. The nose and cheeks were swollen and there was conjunctival and pericorneal injection of the left eye. The right nostril was obstructed and there was a yellow serous discharge. The submandibular lymph nodes were enlarged, firm, and tender, the right one feeling about the size of a golf ball. The upper nodes of the deep cervical chain on the right were slightly enlarged, but there was no other lymphadenopathy. There were no other clinical findings at this time. She had been receiving 1,000,000 units of penicillin daily for ten days without benefit and was now running a low-grade fever. *X*-ray examination revealed both antra clear and no abnormality in upper or lower jaws.

Progress

A piece of gum lesion was removed for histological examination. The report was: "A granuloma with pleomorphic cytology including multinucleate giant cells of the Langhans type; hyperplasia of the covering squamous epithelium with micro-abscesses at the apices of some of the papillae. The appearances are not unlike those seen in hypertrophic gingivitis of pregnancy." Sections were stained by Ziehl–Neelsen and periodic-acid–Schiff techniques without revealing anything further (Special Plate, Fig. 1).

By July 6 the patient was worse. The submandibular nodes were larger, the nose was painfully swollen, and completely blocked by congested mucosa and a shaggy ulcerating granulomatous lesion involving the inferior turbinates. Antral radiographs showed a triangular density in the lower lateral angle of the right antrum. A further biopsy was performed; the histology was the same as before. Aureomycin, 250 mg. four-hourly, was given.

From the beginning of July the urine contained a trace of albumin and the deposit occasional red cells. On July 14 it reduced Benedict's solution; the blood sugar was 340 mg. per 100 ml. A glucose tolerance test showed a diabetic curve: fasting, 220 mg. per 100 ml.; at 30 minutes, 240 mg.; at one hour, 250 mg.; at 90 minutes, 300 mg.; and at two hours, 350 mg. At this time blood examination showed a rising leucocytosis and falling haemoglobin level and red cell count. Repeated blood culture failed to grow any organism; the Wassermann and Kahn reactions were negative; a Mantoux test was negative with 1 in 100 old tuberculin; and the serum was negative for antibodies to enteric organisms and *Brucella abortus*. A vesicular eruption broke out in a small area over the right deltoid, and a biopsy of this was taken. Sections showed subcutaneous haemorrhage beginning to organize, but no evidence of vascular disease. Again Ziehl–Neelsen and periodic-acid–Schiff staining techniques gave no further information (Plate, Fig. 2).

By July 20 the granulomatous lesions were diminishing and the secondary infection was subsiding. On July 22 the serum proteins were 6.15 g. per 100 ml., with albumin 1.73 g. and globulin 4.42 g. per 100 ml. Serum bilirubin was 0.9 mg. per 100 ml. By July 26 the mouth and nose lesions had almost completely resolved, the nose was clear, the facial swelling had subsided, and the conjunctivitis was no longer present. *X*-ray appearances of skull, chest, and pelvis were normal, and the right antrum was now clear. The patient was still pyrexial and complained of great lassitude and weakness; she was depressed and wept frequently.

On August 5 she was transferred to a medical ward. The mouth was now clean, all signs of the granuloma having disappeared. She was obviously very ill, with fever rising to 101° F. (38.3° C.) at times, and her skin was pale and sallow without icterus. She complained of weakness, of headache, and of discomfort on swallowing. The blood pressure was 190/120 mm. Hg and there was slight oedema of the ankles. All tendon reflexes were greatly diminished. The blood urea was found to be 200 mg. per 100 ml., but the glucose tolerance curve had altered: fasting, 160 mg. per 100 ml.; at 30 minutes, 180 mg.; at one hour, 190 mg.; at 90 minutes, 210 mg.; and at two hours, 190 mg. Serum protein values were the same as before. On August 13 she complained of pain and tenderness in the left loin and became drowsy and disoriented. Blood urea was 300 mg. per 100 ml. Next day she became comatose and died, eight weeks and three days from the onset of the gum lesions.

Blood Picture

Haemoglobin values fell from 15 g. per 100 ml. on admission to 9 g. the day before death. Leucocytosis reached 24,000 per c.mm. during the sixth week; eosinophils never exceeded 5% of the total count. Bone marrow was studied on two occasions without any pathological findings.

Post-mortem Examination

The gross findings were as follows. Small right hydrothorax, no pleurisy, moderate oedema of the lungs. Normal-sized heart with small grey nodules in the myocardium. Moderately enlarged, grossly fatty liver. Moderately enlarged spleen with gross perisplenitis, and cut surface showing many grey nodules of varying sizes, some with central thrombosed vessels, standing out against a dull-red hyaline background. Small fibrosed nodules in the pancreas with haemorrhages. Retroperitoneal haemorrhage around the left kidney. Both kidneys swollen, with tense capsules which on stripping left a glistening mottled surface with petechial haemorrhages. The cut surface showed complete destruction of architecture, small thrombosed vessels surrounded by grey nodules standing out against a glistening background. No gum or nasal lesions could be found.

Histology.—In the lungs there was oedema and mild bronchopneumonic changes. No active arteritis was seen, and in sections stained with orcein–methylene-blue for elastic tissue no healed arteritis, as indicated by segmental rupture of elastic fibres, was demonstrable. In the heart a large branch of a coronary artery showed acute arteritis and was partially blocked by thrombus. There were multiple foci of muscle necrosis in varying stages of replacement fibrosis, some of which contained many inflammatory cells and new capillaries. The liver showed extensive peripheral fatty change with pleomorphic cellular infiltration in the portal tracts without any marked changes in the walls of the branches of the hepatic artery. The spleen was extensively necrosed with little unaffected tissue. There were gross necrotizing changes in the vessel walls and an extensive inflammatory exudate. In the pancreas one area showed acute arteritis with necrosis and another a hyalinized nodule. Post-mortem change made interpretation of the lesions difficult. The salivary gland was traversed by intersecting bands of fibrosis with infiltration, mainly lymphocytic and plasma-cell, of remaining parenchyma.

In the kidney there were areas of acute necrosis, and elsewhere oedema and pleomorphic cellular infiltration, mainly polymorphs, eosinophils, and histiocytes, which varied in intensity from place to place and was associated with foci of acute arteritis in medium- and large-sized vessels. There was necrotizing glomerulitis with progressive shrinkage of glomerular tufts and periglomerular fibrosis. Necrosis of tubular epithelium appeared mainly in the proximal convoluted tubules, but owing to the extent and severity of the renal lesions the region of maximum severity was difficult to determine (Plate, Fig. 3).

Discussion

This case was essentially one of periarteritis nodosa with predominance of upper respiratory lesions at onset. These lesions were not invasive or destructive, and resolved before the periarteritis terminated in uraemia. They were,

however, of a granulomatous nature with numerous giant-cells—a picture that has been associated with "malignant granuloma" and "Wegener's granulomatosis."

Godman and Churg (1954) are of the opinion that "Wegener's granulomatosis" and "granuloma gangraenescens" (malignant granuloma) are closely related conditions. These authors were able to study one case of the latter disease of slow progressive course in which at necropsy recent arteritic lesions were found. They also note with interest that in the case of "Wegener's granulomatosis" of longest duration—48 months—only minimal vascular lesions were present *post mortem*. One of their patients is receiving maintenance doses of cortisone and antibiotics nearly three years since he presented with destructive sinusitis and pulmonary granulomata and nephritis.

Summary

The case history of a woman of 41 years who presented with granulomatous rhinitis and gingivitis and died in uraemia after a seven-weeks illness is reported. Necropsy and histological examinations revealed necrotizing glomerulonephritis and lesions of "periarteritis" in many organs, but absent from the lungs.

The relationship between "periarteritis nodosa" and periarteritis with granulomatous lesions is briefly discussed. The general occurrence of pulmonary lesions in the latter syndrome is noted.

Attention is drawn to a recent survey of "Wegener's granulomatosis" and the possible relationship of this condition to "malignant granuloma."

I am indebted to Dr. D. H. G. MacQuaide, Mr. W. C. Gledhill, and Dr. R. H. Heggie for permission to report this case; to Dr. G. Hollingsworth for radiological reports; to Dr. W. E. Bryan for biopsy reports and post-mortem histology, and for assistance and advice; and to Dr. R. B. Coles for his interest and encouragement in the preparation of this report.

REFERENCES

Godman, G. C., and Churg, J. (1954). *Arch. Path.*, **58**, 533.
Howells, G. H., and Friedmann, I. (1950). *J. clin. Path.*, **3**, 220.
Klinger, H. (1931). *Frankfurt. Z. Path.*, **42**, 455.
Kussmaul, A., and Maier, R. (1866). *Dtsch. Arch. klin. Med.*, **1**, 484.
Lindsay, S., Aggeler, P. M., and Lucia, S. P. (1944). *Amer. J. Path.*, **20**, 1057.
Mönckeburg, J. C. (1905). *Beitr. path. Anat.*, **38**, 101.
Ophüls, W. (1923). *Arch. intern. Med.*, **32**, 870.
Stratton, H. J. M., Price, T. M. L., and Skelton, M. O. (1953). *British Medical Journal*, **1**, 127.
Veszprémi, D., and Jancsó, M. (1903). *Beitr. path. Anat.*, **34**, 1.
Wegener, F. (1936). *Verh. dtsch. path. Ges.*, **29**, 202.
—— (1939). *Beitr. path. Anat.*, **102**, 36.
Zeek, P. M., Smith, C. M., and Weeter, J. C. (1948). *Amer. J. Path.*, **24**, 889.
—— (1952). *Amer. J. clin. Path.*, **22**, 777.

The fortieth annual report of St. Dunstan's, *Forty Years On*, gives an account of the work of St. Dunstan's for the war-blinded since its inception. Some 5,000 Servicemen and a few Home Guards and Civil Defence workers have come to St. Dunstan's for training and rehabilitation. To-day a total of 2,600 St. Dunstaners are living—1,450 from the first world war and 1,150 from the second. 58 new cases, including 27 from the second world war, recent casualties from Malaya, Korea, and East Africa, and men from 1914–1918 who have gradually gone blind from mustard gas poisoning, were received last year. Experience has proved that those who come to St. Dunstan's in the early days of their blindness readjust themselves quickest to their new condition, and that neither home nor hospital is the best place for such adjustment. As many blind people have administrative and executive posts and help in the teaching and welfare departments at St. Dunstan's, newcomers are taught by example how to reconcile themselves to their deprivation. To-day, 120 war-blinded are chartered physiotherapists, 140 telephone operators, 100 and more shopkeepers, 550 industrial workers, and some are doctors, solicitors, company directors, and welfare officers.

MALIGNANT CHANGE IN ERYTHEMA AB IGNE

BY

G. A. GRANT PETERKIN, M.B.E., M.B.
F.R.C.P.Ed.
Physician-in-charge, Skin Department, Royal Infirmary, Edinburgh

[WITH SPECIAL PLATE]

The reddish-brown marbling on the skin of the lower legs often found in women who sit long in front of a fire is so common in Britain that it is taken as a matter of course and little attention is paid to it in our textbooks of dermatology. In these it is dismissed in a few lines as erythema ab igne or ephelis ab igne, though the word *ephelis* (freckle) is wrongly used. Hartzell (1912) pointed out that the disease is essentially an inflammatory change and not simply a discoloration of the skin with blood pigment.

Possibly because of the ubiquity of central heating, the dermatosis appears to be rare in the United States, for Hartzell (1912) remarked that cases he has shown at meetings had not been diagnosed by competent dermatologists. He stated that "English dermatologists are apparently the only ones who see it with any degree of frequency." In the same paper he described four cases of this disease and observed that none of the patients were in good health—a significant point. It seems likely that the condition is still often unrecognized in the U.S.A., for Hyman (1954) in discussing a case shown at the New York Academy of Medicine as purpura annularis telangiectodes (Majocchi's disease) remarked that "the lesions are neither annular nor telangiectatic. So the two important features of Majocchi's disease are lacking. In England one often sees this peculiar kind of mottling of the skin, with nothing telangiectatic about it at all, known as erythema ab igne and due to sitting in front of the fire."

In the standard French textbooks, such as the *Précis de Dermatologie*, no reference to the disease can be found, though Erasmus Wilson (1863) quoted Rayer, who described "ephelis ignealis in women sitting over charcoal burners, the histological appearances being those of congestion followed by chronic inflammatory thickening, and even vesication and considerable pigmentation is produced."

In Algiers, Montpellier (1921) described this same reticulate condition as occurring on the inner aspect of the thighs in Moslem women from the use of a little charcoal heater held between the thighs in winter.

But erythema ab igne is probably most common in the colder parts of Asia; for instance, in Kashmir, in cold weather the inhabitants carry beneath their clothing a warming-pan or *kangri*, the temperature of which may reach 150° F. (65.5° C.). Neve (1910) described *kangri* cancer which followed heat burns similar to erythema ab igne. Within a period of fifty years Neve (1929) saw more than 2,000 cases of such cancers. Similar to these is the reaction seen in some parts of China where the people sleep on a heated brick bed or *kang*, so that the skin over the trochanter is burned and *kang* cancer, as described by Laycock (1948), may be provoked. An editorial in the *British Medical Journal* (1954) on "Skin Cancer and Burns" refers to these cancers, and to others such as the well-known carcinoma of the lips in clay-pipe smokers.

It is therefore not altogether unexpected that the erythema ab igne seen in this country should occasionally be the site of squamous-cell carcinoma, and since 1951 I have had four patients with erythema ab igne in which a squamous-cell carcinoma has developed. Because of the frequent occurrence of this unsightly marking of the legs in elderly, middle-aged, and even youthful females in Britain, it was confidently expected that such malignant changes would have been previously described in some book or article, but searching has failed to reveal any such picture.

Description of Cases

Case 1.—A woman aged 71 was first seen in May, 1951, with a particularly severe erythema ab igne, which had been present for years, and a hypertrophic ulcerated area of the left leg, present since September, 1949. A biopsy from the tumour was reported on as follows: "The section consists of the edge of an ulcer bordered by acanthotic epidermis. The floor of the ulcer shows a dense chronic inflammatory infiltrate that almost obscures a low-grade squamous-cell carcinoma. The acanthotic epidermis shows no increase in pigment, the upper dermis is oedematous, the vessels widely dilated, and there is a mild chronic inflammatory reaction round some of the vessels." The Wassermann reaction was negative. The patient was a thin, tired woman with a noticeable reticular pigmentation and telangiectasis on the sides and V of the neck, and erythemato-squamous patches on the brow, nose, cheeks, and tips of the fingers not unlike lupus erythematosus, except that there was no atrophy. A diagnosis of poikilodermia atrophicans vasculare (Jacobi) with erythema ab igne and squamous-cell carcinoma was made. This case was among those shown at a meeting of the North British Dermatological Society on December 13, 1951. Early in January, 1952, the carcinoma was excised and the raw area grafted.

Case 2.—A spinster aged 80 developed an adenocarcinoma of the left breast which was removed surgically in 1942; this was followed by deep *x*-ray therapy, and there has been no sign of recurrence. Apart from this she has been healthy. For many years she had been in the habit of huddling over a big coal fire in the winter, but when she noticed marked "fire-burns" she placed a board and a rug between her legs and the fire. Gradually the pigmentation and redness faded, leaving warty excrescences. In July, 1952, she was referred to me by Dr. Anna Herdman for treatment of a tumour which had grown on one of the warty lesions on her right shin and had reached a diameter of 2 cm. with early ulceration. A biopsy showed a moderately differentiated squamous-cell carcinoma, which was removed by thorough curettage followed by electrocautery. When this area had healed it was treated with *x* rays (2,000 r). She remained under observation. In February, 1955, the irradiated area was still healthy, but another squamous-cell carcinoma had developed on the other leg, and this was treated in the same way.

Case 3.—A woman aged 57 was admitted to the Skin Department of the Royal Infirmary, Edinburgh, on September 7, 1953, with multiple hypertrophic ulcerating tumours of the inner aspects of the thighs and lower legs, situated on areas of skin affected by a chronic erythema ab igne. She confessed that for years she was accustomed to sitting close to a coal fire and realized that this was responsible for her condition. The tumours had gradually developed over the past three years. Her skin was pale, very fair and fine, with almost complete absence of axillary and pubic hair, so as to suggest an ectodermal defect. On the sides of her neck was a reticulate pigmentation with telangiectasia but no true atrophy, and suggested poikilodermia atrophicans vasculare of the Thomson type rather than of the Jacobi variety. Histological examination of tissue removed from several of the tumours showed squamous-cell carcinoma. The tumours were treated by deep *x*-ray therapy, and all vanished satisfactorily except one on the right and one on the left leg, each measuring 3.5 cm. in diameter. The patient was therefore transferred to the care of Mr. A. B. Wallace, plastic surgeon, who excised the carcinomata and grafted the raw areas. (See Figs. A and B.)

FIG. A.—Case 3: Showing erythema ab igne with hyperkeratotic areas and squamous-cell carcinoma.

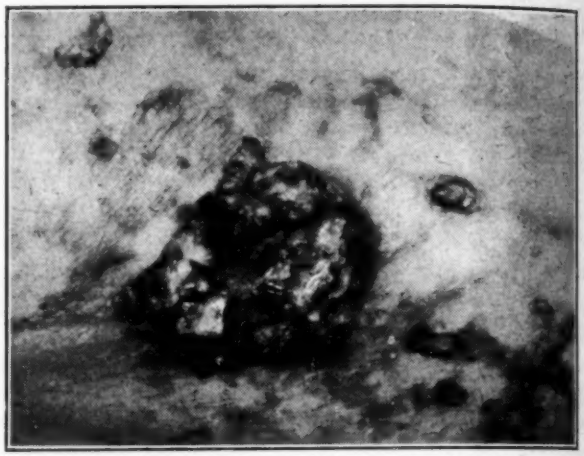


FIG. B.—Case 3: Close-up of squamous-cell carcinoma.

Case 4.—A woman of 56 was sent to see me by Dr. A. E. Turnbull on June 5, 1954. For many years she had noticed discoloration of the skin, chiefly of the left leg, and realized that this was due to her "sitting on top of" a coal fire. As she sat to the right of it the left leg was more scorched than the right. About three years ago she observed a warty area on the marbling of her left leg, and this gradually increased in size. Her previous medical history is of no interest except that in 1946 a malignant ovarian cyst was removed, and following this she received deep *x*-ray therapy. Since then there has been no evidence of recurrence, but her left leg has been slightly oedematous from time to time.

C D

FIG. C.—Case 4: Erythema ab igne with squamous-cell carcinoma of left calf. FIG. D.—Case 4: Infra-red photograph showing retiform pigmentation over deep veins.

The clinical appearance of the condition is shown in Fig. C, and an infra-red photograph for comparison in Fig. D. A biopsy was interpreted by Dr. R. F. Ogilvie, senior lecturer in pathology, Edinburgh University, as follows: "The cutis is very oedematous, markedly infiltrated with polymorphs, round cells, and siderophages in varying proportion, and characterized by a formation of highly vascular granulation tissue. The overlying epidermis is slightly raised and covered by a distinct cornified layer, while masses of keratin plug the epidermal crypts. Bacterial masses are present among the cornified material, and the epidermis as a whole is slightly infiltrated with polymorphs. The Malpighian layer is sprinkled with mitotic figures and includes numerous feebly stained cells, but is not significantly thickened. In other words, no evidence of malignancy is present in the section. The features are those of an organizing subacute inflammatory condition accompanied by some hyperkeratosis." (See Special Plate, Fig. 1.)

The patient was admitted to hospital on July 15, 1954, and a small hyperkeratotic nodule excised from her right leg showed the following picture: "The epidermis is normal in thickness at one end of the section, but becomes progressively thicker in the nodular region. Both Malpighian and cornified layers share in the thickening. The rete pegs in particular are distinctly elongated and characterized by a swollen and actively dividing condition of their cells. Some parakeratosis is also apparent at the nodular end. The corium shows oedema, infiltration with round cells, polymorphs, and siderophages, mainly the first, and formation of vascular granulation tissue, but these features are more marked at the nodular end than elsewhere. The thickened cornified layer at the nodular end is also locally infiltrated with polymorphs. No malignancy, however, is present in this section. The condition is erythema ab igne of particularly marked degree at the nodular end and here accompanied by conspicuous reactive epidermal thickening." (Plate, Fig. 2.) Another biopsy was taken from the tumour on the left leg, of which Dr. Ogilvie reported: "The section shows: (i) the features of well-marked erythema ab igne with reactive epidermal thickening as described for the nodular area in the previous section; and (ii) invasion of the tissue at one end of the section by a moderately differentiated squamous carcinoma." (Plate, Figs. 3 and 4.)

The carcinoma was excised at the plastic unit of Mr. A. B. Wallace and thick razor grafts applied.

Another case of erythema ab igne exemplifies the same reaction (precancerous changes) as that seen in the section taken from the small hyperkeratotic nodule of the right leg in Case 4.

Case 5.—A woman of 77 was referred to me by Dr. A. Y. Cochrane on November 6, 1953. For many years she had had an erythema ab igne affecting the left leg only, and 12 years ago relinquished her habit of sitting over a coal fire. In August, 1953, she observed that an exudative crusting was developing on the "fired" area, and this soon became a heaped-up ulcerated growth. The presence of a squamous-cell carcinoma was suspected, and the tumour was removed by curettage and the base thoroughly destroyed by electrocautery. Section of the lesion showed no evidence of carcinoma, the histological report being: "A keratosis. Much of the epidermis is acanthotic, but the normal cellular architecture is retained. There is a diffuse chronic inflammatory reaction in the dermis. The epidermis is obviously unstable, but no definite malignancy was seen." The skin healed satisfactorily in a little over four weeks, and there has been no recurrence nor have fresh tumours arisen. Apart from a fissure-in-ano her general health has always been good.

Discussion

In taking the history of a patient with squamous-cell carcinoma one is frequently informed that the growth appeared subsequent to a minor injury to the affected part —a point which sometimes has to be considered in industrial compensation. More often, however, these carcinomata tend to appear after repeated minor insults to the skin, so that the appearance of an epithelioma on the site of chronic irritation is a well-known phenomenon, as witness the high incidence of skin cancers in sunny countries such as Australia and South Africa, or the fungating tumours that used to be only too frequent in chronic lupus vulgaris.

The heat-burns due to the *kangri* pot and the *kang* bed have also produced their quota of carcinomata in Asia, and the precarcinomatous lesions in these cases are indistinguishable from erythema ab igne, which has also been reported as due to prolonged application of a hot-water bottle to the abdomen or back. Surprising features of the cases here described are: (1) there appears to have been no previous description of similar cases in any medical book or journal, despite the high incidence of erythema ab igne in this country; and (2) in this small number two of the four patients with carcinoma had been cured of cancer of other organs some years previously, while the other two had skin changes compatible with a diagnosis of poikilodermia atrophicans vasculare, a disease which may be the first sign of an internal carcinoma, leukaemia, or mycosis fungoides, but may also be found in subjects with hereditary ectodermal defects, such as existed in Case 3. Exposure to sunlight and to cold seems to have played a part in some cases of this type of poikilodermia, and Downing *et al.* (1947) have suggested that physical factors might well be precipitating factors.

In the cases now presented the disease began as an acute erythema, sometimes with vesiculation, following exposure to the heat of a coal fire. This erythema died down and recurred repeatedly after numerous similar experiences. Gradually a retiform pigmentation appeared on the skin over the deep veins, as shown by infra-red photography (see Fig. D). After years of such incidents, hyperkeratoses appeared on the dusky-red pigmented areas, as can be seen around the tumour in Figs. A and B. These successive processes ranging from a chronic inflammatory reaction to squamous-cell carcinoma are shown in the histological reports on Case 4 and the photomicrographs (Plate, Figs. 1–4).

It may be impossible clinically, and even histologically, to distinguish when a tumour such as those described has ceased to be a pseudo-epitheliomatous hyperplasia and has become a true squamous-cell carcinoma. In Case 5 the growth appeared to be a hyperplasia only, as serial sections showed no real invasion and comparatively few mitoses, but no doubt it was a precancerous lesion. The carcinomata which developed in these cases were of low malignancy with no evidence of secondary spread, so that the prognosis appeared to be good.

Though erythema ab igne is extremely common in women in Britain, it does not seem to be of frequent occurrence in other parts of Europe, and is decidedly rare in America. This may be accounted for by the universality of central heating, though there are still plenty of coal fires in use in the United States. Any form of heat, if the exposure is long enough, would probably produce the disease, and there is some evidence that erythema ab igne has been provoked by gas and electric fires. It would almost seem as if the inhabitants of North America were not so prone to develop this type of reaction, for Danto and Maddin (1954) described the case of a woman in Vancouver who had developed what they termed "thermal telangiectasia" caused by an electric fire, an electric heating pad, and a car heater. This patient developed numerous discrete, pinhead-sized telangiectases on the posterior aspect of her legs, with no sign of hyperpigmentation, freckling, or mottling. One cannot help thinking that in Britain this person would have shown a typical erythema ab igne.

During a long experience with out-patients, I have observed many women with erythema ab igne, some in the early twenties, but mostly over the age of 40. I have not yet seen a single case of the disease in a male, even though many have confessed to the habit of sitting huddled over a fire for long spells. It may be that endocrine factors play some unknown part in the production of the lesions.

Summary

The chronic inflammatory changes of the skin known as erythema ab igne, due to prolonged sitting over a fire, are common in this country but rare in the United States.

Similar cutaneous changes due to the heat from the *kangri* bowl in Kashmir and the *kang* bed in China have been shown to produce cancers.

Four cases are described in which the patient has developed a squamous-cell carcinoma on an area of erythema ab igne, and one case in which there were premalignant changes. Two of the four patients had been treated for, and cured of, cancer of other organs some years previously; the other two showed the cutaneous changes known as poikilodermia atrophicans vasculare, sometimes found in association with malignant disease.

Acknowledgments are due to Mr. T. C. Dodds, Photomicrography Unit, Edinburgh University; and to Mr. L. A. Jolley, Librarian, Royal College of Physicians, Edinburgh, for his help in searching the literature.

REFERENCES

British Medical Journal, 1954, 1, 204.
Danto, J. L., and Maddin, W. S. (1954). *Arch. Derm. Syph. (Chicago)*, 70, 667.
Downing, J. G., Edelstein, J. M., and Fitzpatrick, T. B. (1947). Ibid., 56, 740.
Hartzell, M. B. (1912). *J. cutan. Dis.*, 30, 461.
Hyman, A. B. (1954). *Arch. Derm. Syph. (Chicago)*, 70, 839.
Laycock, H. T. (1948). *British Medical Journal*, 1, 982.
Montpellier, J. (1921). Quoted by C. du Bois, *Ann. Derm. Syph. (Paris)*, 2, 83.
Neve, E. F. (1910). *British Medical Journal*, 2, 589.
—— (1929). *Practitioner*, 122, 355.
Wilson, W. J. E. (1863). *Diseases of the Skin*, p. 599, Churchill, London.

PNEUMATOSIS CYSTOIDES INTESTINALIS

REPORT OF A CASE

BY

J. D. GRIFFITHS, M.B., B.S., F.R.C.S.

AND

D. F. ELLISON NASH, F.R.C.S.
St. Bartholomew's Hospital

[WITH SPECIAL PLATE]

Cases of gastro-intestinal pneumatosis have been reported in the literature from time to time. The condition was known to John Hunter, who described its occurrence in swine. There is a specimen in the Hunterian Collection of the Royal College of Surgeons: this was sent to John Hunter by Jenner and the gas from the cysts was analysed by Cavendish; a description of the specimen is to be found in Hunter's *Works* (Nitch, 1923). The first reference to the condition in man is in the catalogue of the Anatomical Museum of Amsterdam in 1737 (quoted by Lamont, 1929), where it describes "a portion of jejunum of a man showing a tumour which arose from wind." Bang described the condition in 1876 and Mayer in 1825, the latter calling it emphysema bullosa. Since then there have been many descriptions and much discussion in the literature as to the possible aetiology of these gaseous cysts in the abdomen. Jackson (1940) collected 171 cases from the literature and described one personal case. There have been over 17 further cases reported (Somerville, 1951).

The case now described is of interest because of the confusion caused by air cysts around the terminal ileum, which had become displaced and lay in a suprahepatic position under the right diaphragm.

Aetiology

The association of pneumatosis cystoides with pyloric stenosis is well known. Berglund (1939) states that in 60% of the cases described in the literature pyloric stenosis has been present. Lamont (1929) claims that 50% of cases are definitely associated with duodenal or gastric ulcer.

The aetiology was first fully reviewed by Nitch in his presidential address to the Section of Surgery of the Royal Society of Medicine (1923). He collected 85 cases from the literature, analysing the aetiological factors, and described two cases of his own.

Many theories have been put forward. Neoplastic, bacterial, and mechanical factors have been considered. Eveleth and Biester (1938) discovered that in hogs fed on polished rice cysts developed on the serosa of the intestine. This led many observers to suspect malnutrition as being the main causative factor in this disease. Schorr *et al.* (1951) drew attention to the fact that patients with this condition were usually undernourished, owing mainly to the long history of associated peptic ulceration and subsequent pyloric stenosis. If the pyloric stenosis is relieved the cysts tend to regress immediately, and have been observed to do so by Berglund (1939) both radiographically and by laparotomy. The disease affects infants, and Moore (1929) reported four cases of pneumatosis in infants who died of enteritis with ulceration. Botsford and Krakower (1938) also reported six cases occurring in children in association with diarrhoea or vomiting; no mucosal defects were found on necropsy in these cases. Morison (1952), in discussing the pathology of this condition in infancy, postulated that some of the gas might have been produced by micro-organisms invading the tissues before or after death.

Various authors have suggested that gas is driven into the lacteals through mucosal ulcers, and that the raised intra-abdominal pressure from repeated vomiting might lead to gaseous distension of lacteals.

Case Report

A man aged 51 was brought to St. Bartholomew's Hospital after having collapsed on the platform of a railway station. He complained of severe upper abdominal pain, worse on the right side. He was shocked, dehydrated, and vomiting blood. He gave a 20-year history of dyspepsia, having had a course of medical treatment in hospital 19 years ago for peptic ulcer. Four years ago he was operated on at another hospital for perforated gastric ulcer; the records show that no other abnormality was found in the abdominal cavity. Since this time he had developed two distinct types of pain, one coming on 1½ hours after meals and situated in the epigastrium, and the other in the right hypochondrium which radiated to the back and right shoulder and was not associated with meals. There was a weight loss of 4 stones (25.4 kg.) and he had been unemployed for four years (since his operation for perforation) on account of his disability. Recently repeated vomiting had developed and he had noticed melaena stools on several occasions. Since his operation he had suffered from very severe bronchitis, which had become worse in recent months.

Three days before admission he experienced sudden epigastric pain which persisted; 48 hours later the pain became worse and colicky. He vomited altered blood on four

occasions, and collapsed one hour before admission. He vomited a further litre of altered blood very soon after admission.

The patient was very thin and in a state of shock. Pulse rate, 85 per minute; blood pressure, 115/70 mm. Hg; respirations, 18 per minute; temperature, 97° F. (36.1° C.). The teeth were carious and there was gross gingivitis. The chest was barrel-shaped with poor movement but good air entry; breath sounds were vesicular with moist rales at the lung bases; heart sounds were normal. On abdominal examination a right upper paramedian scar was seen. There was visible peristalsis in the lower abdomen, but no distension. In both upper and lower right quadrants there was marked rigidity, with tenderness in the epigastrium and complete absence of liver dullness; a marked succussion splash could be elicited; bowel sounds were reduced. There was no abnormality on rectal examination.

A radiograph revealed the presence of "loculated" air under the right dome of the diaphragm (Special Plate, Fig. 1). A large portion of intestine was seen extending up the right lateral aspect of the abdomen to lie above the liver. At the time the significance of this subphrenic gas shadow was not appreciated, and the most probable diagnosis seemed to be pyloric obstruction with haematemesis and perforation of a peptic ulcer. A further litre of altered blood and food residue was removed by tube from the stomach. Laparotomy was then performed.

The abdomen was opened through a midline incision. There was no free fluid or gas in the peritoneal cavity. The stomach was grossly distended and occupied both left quadrants, extending into the pelvis (see Plate, Fig. 2, opaque area marked *b*). Above the liver, on the right side, there was a large cystic mass attached to the under surface of the diaphragm. The terminal ileum passed up over the liver into this cystic mass. There was no evidence of any intestinal obstruction. The mass was separated from the diaphragm and the liver, when it was seen to be composed of hundreds of gas-containing cysts surrounding the lower ileum for a distance of 45 cm. (Plate, Fig. 2). The mesentery of the affected part of the ileum was also involved, with cysts ranging from 0.5 cm. to 5 cm. in diameter. Both the caecum and large intestine were unaffected. Owing to the extensive involvement of the terminal ileum and mesentery by the air cysts and absence of involvement of any other part of the gut it was decided to resect the affected segment with its mesentery, leaving a 3-cm. stump at the ileo-caecal end and performing an end-to-end anastomosis. There was an ulcer mass with considerable oedema in the region of the pylorus, but no sign of recent perforation. Partial gastrectomy seemed inevitable owing to the presence of pyloric obstruction and haematemesis, and was performed with the Moynihan II method.

The patient made a good recovery. His general condition improved rapidly and he had no further bronchitis. *X*-ray examination of the chest showed areas of cystic emphysematous changes at both lung bases. He has now been able to return to light work and is free from pain for the first time for 25 years.

It seemed likely that the cystic loop of bowel above the liver might have become displaced during cleansing of the subphrenic pouches at the operation for closure of the perforated duodenal ulcer four years previously.

Pathological Report

The specimen consisted of approximately 75 cm. of ileum showing numerous thin-walled, translucent cysts varying from 2 mm. to 3 cm. in diameter distributed along its length. The cysts were most numerous about the central portion of the excised ileum, and here the affected gut was coiled upon itself and continuous loops and cysts were adherent to one another, forming an irregularly nodular mass. Less-affected lengths of ileum projected. The cysts, containing gas, were present beneath the mucosa (which was not ulcerated), in the substance of the muscularis, and beneath the serosa, along both mesenteric and free borders. The main nodular mass was purple-red in colour and congested. The attached mesentery was oedematous and hyperaemic and packed with cysts, many of which were several centimetres from the bowel.

Sections of small intestine showed a number of empty cystic spaces in the submucosa, muscle coat, and particularly in the rather fibrosed subserosal layer. Some cysts had little lining endothelium, while others had a layer of cubical flattened endothelium. In yet others a number of large giant cells were incorporated in the lining endothelium. Sections of lymph nodes showed only sinus catarrh.

Sections of stomach revealed the presence of an active chronic peptic ulcer.

Discussion

Cystic pneumatosis may be found associated with any part of the intestine. It is commonest in the jejunum (Lamont, 1929), but a number of cases have been described where the cysts occurred in the distal ileum. Pybus (1934) reports such a case which resembles the one described above, though in his case cysts were also present in the falciform ligament of the liver. Jones (1948) describes pneumatosis occurring in the large gut in association with a chronic volvulus of the sigmoid colon. Cysts have also been seen at sigmoidoscopy, looking like small grapes, which when ruptured were found to contain gas. Sherwin and Messe (1952), reviewing the American literature, found reports of only 43 previous cases. They added a further case which bears a striking similarity to that now described. Their patient had pyloric obstruction due to peptic ulceration, and the affected loop of ileum was wedged between the dome of the diaphragm and the liver on the right; cyst formation extended to within 6 in. (15.2 cm.) of the ileocaecal junction.

One of the complications of this condition is pneumoperitoneum, due to rupture of the cysts, as described by Somerville (1951), Schorr *et al.* (1951), and Jones (1948). It may be the presenting clinical feature. Pneumomediastinum has also occurred.

It is known that these cysts can disappear spontaneously after relief of the causative factors, but remaining cysts may give rise to post-operative pneumoperitoneum and other complications (Berglund, 1939). The mass of cysts can cause intestinal obstruction due to pressure on the intestinal tract, as described by Thoma and Hennigar (1952). It has been suggested that subserous cysts are of a precancerous nature, although this association is not generally accepted.

If the cysts are localized to one area of the bowel and a laparotomy has been performed, it would seem correct to excise the area containing them. Any coexistent gastric, duodenal, or intestinal condition must be dealt with appropriately as the primary treatment. Excision avoids the possible complication of pneumoperitoneum and intestinal obstruction which may arise subsequently from progressive inflammatory change and fibrosis.

Summary

A case of ileal pneumatosis cystoides which developed in association with prolonged malnutrition due to chronic gastric ulcer is described. The presenting symptoms were due to haemorrhage from the ulcer. The presence of gas below the diaphragm led to a mistaken diagnosis of perforation of the ulcer. Partial gastrectomy and excision of affected ileum relieved the patient's symptoms so that he was able to return to full employment after four years' disability. It is suggested that the affected ileal loop had been displaced to the anterior subphrenic pouch at a previous operation; its fixation here and its subsequent exposure to continuous variations in pressure between liver and diaphragm may explain the localization of the pneumatosis.

There seems little doubt that violent changes of intra-abdominal pressure caused by vomiting have some connexion with the production of this condition. Vomiting so often occurs in association with chronic malnutrition that a nutritional factor may also be operative.

We wish to acknowledge with gratitude the generous help of the Pathological Department of St. Bartholomew's Hospital.

REFERENCES

Bang, B. L. F. (1876). *Nord. med. Ark.*, **8**, No. 18, 1. (Quoted by Lamont.)
Berglund, S. (1939). *Acta radiol. (Stockh.)*, **20**, 401.
Botsford, T. W., and Krakower, C. (1938). *J. Pediat.*, **13**, 185.
Eveleth, D. F., and Biester, H. E. (1938). *Amer. J. Hyg.*, **27**, 364.
Jackson, J. A. (1940). *Surg. Gynec. Obstet.*, **71**, 675.
Jones, J. D. T. (1948). *Brit. J. Surg.*, **36**, 49.
Lamont, D. (1929). *Glasg. med. J.*, **111**, 283.
Mayer (1825). *J. Prakt. Heilk.*, **61**, 67. (Quoted by Lamont.)
Moore, R. A. (1929). *Amer. J. Dis. Child.*, **38**, 818.
Morison, J. E. (1952). *Foetal and Neonatal Pathology*. Butterworth, London.
Nitch, C. A. R. (1923). *Brit. J. Surg.*, **11**, 714.
Pybus, F. C. (1934). Ibid., **21**, 539.
Schorr, S., Ullmann, T. D., and Laufer, S. (1951). *Arch. intern. Med.*, **88**, 362.
Sherwin, B., and Messe, A. A. (1952). *Ann. Surg.*, **136**, 893.
Somerville, P. (1951). *Lancet*, **2**, 1160.
Thoma, G. W., and Hennigar, G. R. (1952). *Amer. J. clin. Path.*, **22**, 765.

Medical Memorandum

Use of Papaverine in Traumatic Arterial Spasm after Supracondylar Fracture of Humerus

Threatened ischaemia consequent upon fractures in the upper limb has always presented its difficulties, not only of recognition but also of treatment. The following case report illustrates some of the prevailing views held on the treatment of arterial spasm.

CASE REPORT

On March 20, 1954, a 6-year-old boy was brought to the casualty department with a history of having injured his left elbow.

On examination he was pale and in some pain but not obviously shocked. The left elbow was swollen, heavily contused, and deformed, suggesting a supracondylar fracture of the humerus. The proximal end of the humerus was palpable in the antecubital fossa and appeared to be immediately subcutaneous. The radial pulse was impalpable despite prolonged examination and its absence indicated some form of arterial damage. *X*-ray examination confirmed the diagnosis of a severe supracondylar fracture with marked posterior displacement and a less severe lateral displacement of the distal fragment.

One attempt at manipulation of the fracture was made in the casualty department in the hope that adequate reduction would restore the blood supply to the distal part of the limb (Griffiths, 1948). Not only was there a failure to restore the radial pulse, but reduction of the fracture was impossible, and it was clear that the proximal fragment of the humerus had buttonholed the soft tissues. As his fingers were developing a cyanotic tinge and fast becoming cool and swollen, the patient was prepared for transfer to the theatre, where both the fracture and the brachial artery could be explored.

At operation a medial longitudinal incision was made because of the severe soft-tissue swelling. The subcutaneous tissues were found to be severely contused and lacerated. The proximal end of the humerus was found to have buttonholed the brachialis muscle and lay just under the skin in the antecubital fossa, in direct medial relationship to the median nerve, which, however, showed no signs of damage.

Initially the brachial artery was difficult to identify by virtue of the extreme spasm for approximately 12 cm. of its length, which made it resemble one of its own venae comites. When ultimately identified by the recognition of proximal normal pulsation, the vessel was lifted from its bed so far as was technically possible in a vessel so contracted. This procedure produced no obvious change in the condition of the artery, and without further delay a 5% solution of papaverine sulphate was applied superficially to the vessel wall. The response was dramatic. The brachial artery assumed its normal size within two to three minutes, with ample evidence of full and sustained arterial pulsation. The vessel wall appeared undamaged. Reduction of the fracture was not completely successful, for it was virtually transcondylar and very unstable.

The loosely sutured wound was drained and the arm immobilized in a plaster-of-Paris posterior slab and a lateral stirrup. At the conclusion of the operation stellate ganglion and brachial plexus blocks were performed. The radial pulse was now easily palpable at the wrist.

Post-operative treatment included elevation and cooling of the limb. The following morning the radial pulse remained easily palpable; the fingers were warm and the colour was normal. By the same evening the whole limb had begun to swell and the pulse was correspondingly weaker, although the fingers retained their warmth. All dressings were freed, and to ensure maximum vasodilatation of collateral vessels a further brachial plexus block was performed. The pulse none the less continued to be weak and intermittently palpable for the next three days, but at all times the hand remained warm. The view was held that the pulse was difficult to feel owing to the increasing tension created by the injury. Confirmation of this view was provided by inspection of the arm and elbow; for here, in association with the intense swelling, the skin showed the haemorrhagic vesication of impaired viability. Subsequently the wound broke down for this very reason and required skin grafting.

Although his convalescence was slow, he ultimately made satisfactory progress, and when seen six months after the injury there was no evidence of ischaemic changes to be found in the limb.

COMMENT

Griffiths (1948) has shown that, when conservative measures have failed, exploration must be carried out to expose the artery, and, provided there is no arterial damage, the vessel is liberated, mobilized, and, if necessary, a solution of procaine applied. At the conclusion of the operation he advocates sympathetic paravertebral block in the neck, presumably to eliminate spasm in the smaller arteries and in the arterioles.

It has since been shown experimentally by Kinmonth (1949) that smooth-muscle contraction gave rise to local segmental spasm in the large arteries of the body, in the maintenance of which nervous factors did not play a demonstrable part. Following these important findings, Kinmonth (1952) made known the results of directing his attention to paralysing smooth muscle itself by smooth-muscle-relaxing drugs. He found that the local application of papaverine sulphate to the walls of large arteries was the most effective in the volume of its response, in its speed, and in its sustained action.

This case demonstrates the immediate and dramatic effect of papaverine sulphate in relaxing arterial spasm when used locally. In injuries of this nature, where, following exposure of the brachial artery, simple spasm is found, the initial local application of papaverine would appear to be the treatment of choice.

I wish to thank Mr. W. D. Park for his help and for permission to cite this case.

P. ABBEY, F.R.C.S.,
Former Surgical Registrar, King George Hospital, Ilford, Essex.

REFERENCES

Griffiths, D. Ll. (1948). *J. Bone Jt Surg.*, **30B**, 280.
Kinmonth, J. B. (1952). *British Medical Journal*, **1**, 59.
—— *et al.* (1949). *Surgery*, **26**, 452.

Reviews

PHYSIOLOGICAL CHEMISTRY

Cole's Practical Physiological Chemistry. Revised and re-written by Ernest Baldwin, Ph.D., and David James Bell, Sc.D., F.R.S.E. Tenth edition (Pp. 261+x. 21s.) Cambridge: W. Heffer and Sons Ltd. 1955.

The teaching of biochemistry to medical students has undergone important developments during the past twenty-five years. What used to be taught, and called "physiological chemistry" or "chemical physiology," was largely the simple chemistry of proteins, fats, and carbohydrates, blood and excreta, and included tests for normal and abnormal constituents of urine. As knowledge concerning the chemistry of normal physiological function grew biochemistry began to take shape as a subject in its own right, and the teaching of physiological chemistry to the medical student became included in a wider course, usually designated "biochemistry." Biochemistry may be properly defined as the study on a molecular plane of the structure and function of biological systems. Biochemistry as it exists to-day subsumes physiological chemistry, but a differentiation of physiological chemistry from biochemistry is sometimes maintained for traditional purposes.

One may properly ask the question, Where are the limits to be set to the knowledge which the medical student can properly be expected to command? One reasonable answer would be that sufficient groundwork ought now to be covered to enable him, when the time comes, to read intelligently the *British Medical Journal* as it may well be some decades hence. One may safely assume that to-day's study of normal function will provide the basis for the future understanding of the nature of disease, and it is certain that biochemistry will contribute greatly to this development of our knowledge. The student of to-day should be able to face the biochemistry which he will necessarily meet in to-morrow's medical journals with as little fear as is possible. Often it is easy to underestimate and to neglect what is imperfectly understood because of an unsound background knowledge of the subject.

Cole's Physiological Chemistry first appeared in 1904 and had reached its ninth edition in 1933. At this time it was widely acknowledged as one of the best textbooks of its kind in the English language, being based on many years of experience of teaching medical students and containing experiments which could always be relied upon to work. The author's own comments in the footnotes to the descriptions of the experiments were often of delightful significance, being born of an unrivalled experience of the practical tests themselves and the reaction of the average student to them. The particular value of the ninth edition was shown by the fact that it was reprinted three times between 1933 and 1944.

Two of Cole's former colleagues at Cambridge have now collaborated to produce a new edition twenty-two years after the last one. This retains almost unchanged the lucid and valuable first chapter on hydrogen-ion concentration, though naturally most of the rest of the book has undergone extensive revision. It is now perhaps more than ever a practical textbook concerned with the properties of food, of excreta, and of the chemical constituents of the body, with little or no reference to functional biochemistry. The editors make clear in the preface that this is indeed their aim, but whether or not this recidivation is wise in a world illuminated by Professor Baldwin's own *Dynamic Aspects of Biochemistry* remains to be seen.

F. G. YOUNG.

THE LAW ABOUT HEALTH AND WELFARE

Health and Welfare Services Handbook. By John Moss, C.B.E. Second edition. (Pp. 408+xxii. 25s.) London: Hadden, Best and Co. Ltd. 1955.

The origin of this book is Dumday's *Relieving Officer's Handbook*, first published in 1902. It was the textbook used in preparing for their examinations, and their desk companion when in office. The first edition in its new form appeared in 1948, when the legislation became operative which brought to an end the venerable Poor Law service and with it the relieving officer. The book described the various provisions made by Parliament through central and local government to replace the work previously performed by the Poor Law or, since 1930, the Public Assistance authorities.

This new edition is called for because during the last seven years there has been much new legislation and shoals of Ministerial circulars on these subjects. No better person could have been selected for the difficult task of assimilating all this mass of material and presenting it in a digestible form than Mr. John Moss, a barrister and for many years the public assistance officer for Kent. Perhaps inevitably it reads like a law book and is heavily laden with quotations from Acts of Parliament and departmental circulars. Tables giving only the titles of statutes, statutory rules, and leading cases occupy 12 pages.

The book describes in detail the provisions of the National Assistance Act, the National Insurance Act, the Children Act, and those parts of the National Health Service Act which concern local authorities. A chapter is devoted to the residential accommodation provided by local authorities and the division of responsibility between them and hospital boards. The duties of children's officers are well described, and there is much useful information about the placing of foster-children and the law on the adoption of children. Perhaps the most useful chapter for the medical reader is on the mental health service. The intricacies of the law about both the mentally disordered and the mentally defective are set out clearly. The contributions to, and the cash benefits provided by, the National Insurance Scheme are listed, but some are already out of date, as they were increased while the book was in the press. There is an excellent index.

The book will be of value to the medical officer of health, who will be able to find in it at once the reference he may need to an Act of Parliament or an official circular. The clinician who has a copy on his bookshelf will be able by its aid to answer some of the more unusual questions put to him by his patients.

ALLEN DALEY.

ATHEROSCLEROSIS

Symposium on Atherosclerosis. Held under the auspices of the Division of Medical Sciences, National Academy of Sciences, National Research Council, at the request of the Human Factors Division, Air Force Directorate of Research and Development, March 22 and 23, 1954. (Pp. 249; illustrated. $2.) Washington: National Academy of Sciences, National Research Council. 1954.

This monograph contains the papers read at a meeting called at the request of the Human Factors Division of the United States Air Force Directorate of Research and Development. The interest of the Air Force in atherosclerosis arises from the fact that cardiovascular disease is a factor limiting the length of service of flying personnel. It was realized that many of the participants in the symposium would be dealing with fundamental aspects of this disease process, but they were requested to keep the practical problem in the forefront of their discussion. In this they have not been wholly successful.

The symposium is divided into five sections, with a critical summary at the end of each. The first section deals chiefly with the structural changes in the arterial wall which some observers regard as the essential causative factor in atherosclerosis. A. J. Lansing presents data suggesting that the chemical composition of elastin in the media of the large arteries changes with age, and tries to relate this to the amount of available elastase, a pancreatic hormone of islet origin. The second section discusses the reaction of the arterial wall to injury and the role played by local factors in permitting the deposition of lipids in particular areas. The third section is very short and deals with the application of newer physical techniques to the study of

blood vessels. The fourth section, on systemic biochemical factors in the causation of atherosclerosis, is in some ways the most stimulating. A. L. Lehninger gives a masterly summary of present views on lipid metabolism, and R. G. Gould writes on the control of steroid metabolism. Ancel Keys summarizes his well-known views on the important part which diets with a high fat content play in the causation of atherosclerosis. The last section is concerned with the lipoproteins and the evidence that they are involved in the production of atherosclerotic changes in vessels.

The causation of atherosclerosis appears to be almost as difficult to unravel as that of cancer. In both cases we seem to be confronted with a jigsaw puzzle of which some parts are missing, some pictures appear twice in slightly different forms, and others seem to come from an entirely different set. It is to be hoped that soon someone with a more than usually observant eye will be able to see the whole picture. It is clear that no one so far has caught more than a glimpse of a part of it. This monograph shows that failure will arise from lack neither of effort nor of interest. It can be strongly recommended to those interested in the question of the causation of atherosclerosis. It does not include the clinical syndromes arising as a result of atherosclerotic changes in vessels.

E. J. WAYNE.

THE CEREBRAL CORTEX

Studies on the Cerebral Cortex. By Santiago Ramón y Cajal. Translated from the Spanish by Lisbeth M. Kraft. (Pp. 179 +xi; illustrated. 27s. 6d.) London: Lloyd-Luke (Medical Books) Ltd. 1955.

Dr. Kraft undertook the translation of this part of Cajal's classical works because of the need for reference to the cellular structure of the limbic lobe. This is because of the evidence that is accumulating that the limbic lobe, which includes the hippocampus and Ammon's horn, is concerned with visceral activity related to emotional change, and also because it seems to play an important part in determining the response of the hemispheres to environmental changes. As it has for long been known to undergo change in patients with epilepsy, and as the diffuse disturbances occurring in the epileptic attack seemed to be mediated through the midline mechanisms with which it has connexions, it is the focus of intense contemporary interest. Dr. Paul MacLean, with whom Dr. Kraft works, has been engaged for some years in a study of the function of this old and essential part of the brain in lower mammals, and it was he who felt the need to be closely in touch with the histological studies made by Cajal over 50 years ago.

The translation flows freely and its origin assures its accuracy; the text is liberally illustrated with Cajal's original drawings, and on most pages there are footnotes referring to the literature. The book will be used as a source of reference by those who are interested in human and animal behaviour, whose studies take them into the realm of what used to be considered the olfactory brain.

DENIS WILLIAMS.

THALLIUM POISONING

Thallium Poisoning. By J. J. G. Prick, W. G. Sillevis Smitt, and L. Muller. (Pp. 155+vi; illustrated. 19s.) Amsterdam, Houston, London, New York: Elsevier Publishing Company. Distributed in U.K. by Cleaver-Hume Press Ltd. 1955.

Thallium poisoning as an occupational disease has rarely been reported, and, since the use of thallium as a depilatory has been discontinued as a result of reports of poisoning in 1910, this source of intoxication has largely disappeared. Since its introduction in the Netherlands in 1920 as a rat poison, there remains, however, the possibility of its ingestion, either by accident or by design, in cases of suicide or murder. In *Thallium Poisoning* this possibility is fully explored and actual cases occurring in the Netherlands are described in detail.

The minimum lethal dose of thallium for an adult is 0.8 g., and a tablet of the rat poison "celio" contains 1.6–2% of thallous sulphate (more toxic than the trivalent thallic compound). Because it is soluble in water, completely odourless and tasteless, and its ingestion is followed by symptoms of poisoning only after one or two days, it is exceptionally easy to administer a fatal dose without immediate detection. The diagnosis in acute fatal cases, and even more in chronic cases, is difficult, for the symptoms cover a wide range of disorders, including gastro-enteritis, polyneuritis, alopecia, skin lesions, bronchitis, and psychic disturbance, with a peculiar reversal of the sleep rhythm. This difficulty is well exemplified in the description of a case in which the patient suffered from repeated attacks of pain in the epigastrium and in both legs from the age of 9 to 33. During this period he underwent two laparotomies and removal of a normal appendix, and it was not until alopecia of the scalp and eyebrows appeared that the correct diagnosis, supported by the presence of thallium in the urine and faeces, was made. This psychopathic subject had apparently ingested "celio" tablets in small doses as a "reaction to the weariness of life."

The most valuable aspect of the book is the description of the pathology of the central nervous system, with excellent reproductions of the microscopical appearances showing degenerative changes in the ganglionic cells.

ETHEL BROWNING.

A DOCTOR IN THE HOUSE

Doctor in the Whips' Room. By Sir Henry Morris-Jones. (Pp. 211; illustrated. 18s.) London: Robert Hale Ltd. 1955.

Comparatively few general practitioners have gained distinction in the House of Commons. Sir Henry Morris-Jones is one of that select number, and has written quite an interesting autobiography, though we frequently found ourselves wishing that he had given us greater detail of some parts of his life. He was born in a small village in North Wales which he does not name, but describes as "not pretty." He studied medicine at Glasgow, qualified in 1906, spent two or three years doing "locums," served with distinction in the war of 1914–18 (winning the Military Cross), and after the war set up in practice in North Wales. He quickly achieved professional success and saved money, but lost some of it through trusting an untrustworthy adviser. In 1929 he stood for Parliament and was returned as Member for Denbigh, remaining in the House of Commons till 1950. He was Whip in the National Government from 1932 to 1937 and Junior Lord of the Treasury from 1935 to 1937. He took part in two Parliamentary delegations—one to Australia in 1938, and another to Buchenwald in 1945. Altogether he had varied and interesting experiences, met many prominent people, and travelled in many countries.

He writes in an easy style, gives short accounts of a number of celebrities he met, intersperses a few stories, and gives some of his own (sometimes surprising) opinions. One of his stories sticks in the memory. When he was in practice he once wished to count the pulse of a lady patient and said to her, "Give me your hand." She did so and he counted the pulse. The next day he received a letter from the lady in which she accepted his supposed proposal of marriage. He does not say how he explained matters. He would like to see Wales with a Secretary of State of its own who should have a seat in the Cabinet. If he could he would abolish the names Jones, Davies, Hughes, Roberts, Thomas, Williams, and one or two more. He states that Sir Robert Jones once told him that "he thought his surname had delayed his world-wide recognition by many years."

The final chapter deals broadly with the question of retirement. As for the author himself—"My own life for six months after I left the House of Commons was a period of the greatest misery"; he therefore gives good advice to those about to retire.

ZACHARY COPE.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY DECEMBER 31 1955

HEPATIC INSUFFICIENCY

Extensive damage to the liver, as, for example, in portal cirrhosis, is compatible with normal function of liver cells: the disease is then called "well-compensated." Hepatic insufficiency, or hepatocellular failure,[1] results when liver-cell function is impaired and is associated with a number of clinical features resulting from widespread disturbances of physiological mechanisms. The most important of these are jaundice, ascites, fetor hepaticus, and endocrine, circulatory, and neurological changes. Portal cirrhosis is not the only cause of hepatic insufficiency; the syndrome can occur in infective hepatitis and in other forms of cirrhosis. It may be associated with the terminal stages of obstructive jaundice, though it is remarkable how long a patient can tolerate bile-duct obstruction without deterioration in the function of the liver. Interference with the arterial blood supply and occlusion of the hepatic veins (Chiari's syndrome) both lead to liver failure, though portal-vein obstruction does not impair the function of the liver. Bleeding from oesophageal varices is not in itself a sign of hepatic insufficiency, and in patients with extrahepatic portal obstruction the liver is normal. Liver failure may arise insidiously or may be precipitated by alcohol, gastrointestinal bleeding, infections, and operations.

The various forms of hepatic insufficiency are best illustrated by the patient with portal cirrhosis. Ascites in liver disease always implies hepatic insufficiency, and is often accompanied by oedema, oliguria, and jaundice. The serum bilirubin is raised, serum albumin is lowered, and flocculation tests are positive. The lowered serum albumin leads to a fall in colloid osmotic pressure and this appears to be the principal factor in the onset of ascites in certain types of hepatitis.[2] Attempts have been made to determine the critical level of serum albumin in patients with cirrhosis, and J. Post and A. J. Patek[3] give a figure of 3.1 g. per 100 ml. It is well known, however, that ascites may be present at concentrations greater than this, and other factors, such as an increase in portal venous pressure and even in hepatic venous pressure[4] are probably equally important. Whatever the ultimate mechanism, there is little doubt that, as in heart failure, salt retention is responsible for the perpetuation of ascites. The sodium concentration in urine, sweat, saliva, and faeces is negligible, and increased amounts of salt-retaining corticoids, such as aldosterone, have been reported.[5] This abnormality of salt retention provides a basis for the treatment of these patients.

Endocrine changes are also a feature of hepatic insufficiency. These are only partially explained by the theory that the damaged liver fails to inactivate steroid hormones and especially oestrogens.[6] Spider naevi and palmar erythema are perhaps the best known of these signs of liver disease, though they can occur in normal people as well as in pregnant women and in patients with rheumatoid arthritis. For some reason spider naevi are rarely found below the nipple line except on the arms, and this characteristic distribution is difficult to explain on an endocrine basis. Other endocrine changes are gynaecomastia, testicular atrophy, loss of body hair, and menstrual disturbances. The young female with cirrhosis is almost always infertile. Pigmentation and clubbing also result from severe liver disease, though their aetiology is obscure. Patients with cirrhosis may have warm extremities, but do not sweat because of salt retention. A bounding pulse and the presence of capillary pulsation have led to measurements of cardiac output,[7] and this is sometimes increased. The reason for this is not known, but a similar "high output state" may be seen in patients during hepatic coma.

The neurological manifestations of hepatic insufficiency have received more attention recently.[8] They may occur in acute or chronic forms and are characterized by mental and motor disturbances. Changes in behaviour, with confusion and disorientation, may progress to stupor and coma. The coma fluctuates, and it is unwise to give a poor prognosis. A characteristic "flapping tremor" of the outstretched hands may be observed, and this may spread to involve the whole body so that the patient is completely incoordinate. Rigidity and exaggeration of the tendon reflexes are seen, and meningism and epileptiform convulsions can occur. There is often a sweet, musty odour in the breath, which is known as fetor hepaticus and may be a useful sign when the patient is first seen in coma. Fetor hepaticus used to be considered a grave sign, but it is now known to occur

[1] Sherlock, S., *Diseases of the Liver and Biliary System*, 1955, Oxford.
[2] Bjorneboe, M., *et al.*, *Arch. intern. Med.*, 1949, **83**, 539.
[3] Post, J., and Patek, A. J., jun., ibid., 1942, **69**, 67.
[4] Madden, J. L., *et al.*, *Surg. Gynec. Obstet.*, 1955, **99**, 385.
[5] Luetscher, J. A., and Johnson, B. B., *J. clin. Invest.*, 1954, **33**, 1441.
[6] Dohan, F. C., *et al.*, ibid., 1952, **31**, 481.
[7] Kowalski, H. J., and Abelmann, W. H., ibid., 1953, **32**, 1025.
[8] Sherlock, S., *et al.*, *Lancet*, 1954, **2**, 453.
[9] Challenger, F., and Walshe, J. M., ibid., 1955, **1**, 1239.
[10] Walshe, J. M., ibid., 1955, **1**, 1235.
[11] Riddell, A. G., *Postgrad. med. J.*, 1955, **31**, 389.
[12] Atkinson, M., *et al.*, ibid., 1954, **1**, 128.

as a transient feature in patients who are not in coma. The odour is thought to be due to methyl mercaptan and related substances.[9] "Hepatic coma" is believed to be due to poisoning by nitrogenous compounds absorbed from the gut, which either by-pass the liver through extensive portal-systemic anastomoses or are not detoxicated by the damaged liver. The biochemical disturbance is complex, though ammonia appears to play a part, and J. M. Walshe[10] has suggested that there is an interference with ammonia-binding mechanisms in the brain. A. G. Riddell[11] has recently reviewed the mechanism of hepatic coma and made useful suggestions about the management of patients with this condition.

Patients with liver disease must avoid sustaining further damage to the liver. They usually tolerate operations badly, and anaemia and malnutrition must be combated by haematinics and a well-balanced diet. Recent work suggests that high-protein diets, ammonium compounds, and substances such as choline and methionine may precipitate hepatic coma. It is therefore probably both unwise and unnecessary to give excess protein, and methionine and choline should no longer be used in the treatment of liver disease. Alcohol must be forbidden, and sedatives should be used sparingly and in small doses. Infections usually respond best to the newer antibiotics. Regimes based on salt-free diets and mercurial diuretics are often beneficial to patients with ascites,[12] but ammonium chloride should be prescribed with caution. Repeated paracenteses are a drain on protein. Intravenous glucose is useful supportive therapy for the patient in hepatic coma, and Walshe uses large doses of glutamic acid for its ammonia-binding capacity. This drug is valuable in the coma of chronic hepatic insufficiency, but fails to influence the course of massive hepatic necrosis due to infective hepatitis. Although rare, it is this form of hepatic insufficiency which still remains a challenge to the physician's skill in therapy.

EMPLOYMENT OF THE ELDERLY

One of the most interesting of the many problems raised by the ageing of our population turns on the employment of middle-aged and old people. In 1954 a study carried out under the auspices of the Ministry of Pensions and National Insurance[1] showed that six out of every ten men decided not to take their minimum pension at age 65, but to continue at work; and 45% of those who continued said they did so because of financial necessity. For reasons that are obvious enough, official policy tends to welcome the continuation of old people in employment; they may help to expand output in a time of full employment, and, by postponing the age at which they begin to draw retirement allowances, may ease the strain on insurance funds. Some men on reaching the age of 65 are disposed to take their pensions, feeling that they have earned them; some, who might have liked to continue in employment, find the work in which they are engaged to be taxing them too heavily and see little prospect of being able to change to something more suitable. Although under 4% of the men in the Ministry of Pensions study gave "heaviness of work" or "strain" as the reason for retirement, men whose work entailed a possible cause of strain were apt to retire earlier than other men. Unskilled men are usually at a disadvantage. Not for them the sheltered life of the old craftsman, who, in his own time, may well be able to continue to turn out work of a quality and individuality that command a ready market. In heavy industry, such as shipbuilding, some of the more demanding jobs virtually impose a schedule of retirement which, for ordinary mortals, begins to operate long before the age of 65: the skilled men of the yards, no longer able to follow their trade, may be given jobs as gatekeepers, storekeepers, and the like, which at least preserve their contact with the only working life they have known; but there are never enough jobs of the kind to meet the demand, and the unskilled, regarded as having less claim, are unlikely to be able to secure them.

In his study of men engaged in foundry work I. M. Richardson[2] found they were apt to move from heavy to lighter work in their fifties and sixties. More recently, on the other hand, in a study of the job changes of men of different age groups between light and heavy work in a factory making electrical batteries, R. M. Belbin[3] found that the heaviest work was often carried out by the older workers and the lightest by the younger. But, as Belbin himself points out, his results are not altogether comparable with Richardson's. It must be very difficult to establish criteria that will make possible an accurate comparison of jobs by "heaviness." Changes of job in which ill-health was a factor were excluded from Belbin's series but included in Richardson's; and it must often be wellnigh impossible to draw a line, in the case of a man past middle age whose background is heavy industry, between incapacity for work born of, or aggravated by, the aftermath of illness or injury

[1] *National Insurance Retirement Pensions: Reasons given for retiring or continuing at work*, November, 1954, London.
[2] Richardson, I. M., *Brit. J. industr. Med.*, 1953, **10**, 269.
[3] Belbin, R. M., ibid., 1955, **12**, 309.
[4] Thomas, G., and Osborne, B., *Older People and their Employment*, an inquiry made by the Social Survey for the Ministry of Labour and National Service, 1950, London.
[5] MacPhail, A. N., and Ferguson, T., *Glasg. med. J.*, 1955, **36**, 319.
[6] Clark, F. le Gros, and Dunne, A., *Ageing in Industry*, 1955, The Nuffield Foundation, London.
[7] Grant, I. D., *British Medical Journal*, 1955, **2**, 1181.
[8] *Second Report of the National Advisory Committee on the Employment of Older Men and Women*, 1955 (H.M.S.O., 1s. 9d.).

and incapacity due to failing powers associated with advancing years as such. Illness is important in causing change of job at all ages, and, as Belbin says, the mere fact that older people are engaged in heavy work does not necessarily imply their suitability, in terms either of capacity or of performance. G. Thomas and B. Osborne[4] reported that 69% of heavy labourers between the ages of 55 and 74 found their work a strain, and more recently A. N. MacPhail and T. Ferguson,[5] in a study of men who had experienced much unemployment, found that those men in their series who had served an apprenticeship to some trade in earlier life had nearly always fallen out of employment because of severe disability; and the older the age group the greater the importance of disability. In explanation of his findings, Belbin inclined to the view that the preponderance of older men in heavy work was due to the fact that the younger were preferred for the light kinds of work, which often demanded qualities of "nippiness" rather than physical strength; but that when older people had difficulty in maintaining their performance they tended to move, not to lighter occupations, for which there is more competition, but rather away from production work into such ancillary jobs as gate-keeping or night-watching, or to transfer to labouring jobs which, though heavy, sometimes permit a man to work at his own speed.

Le Gros Clark and A. Dunne,[6] basing a study of thirty-one occupations on the tables of age and occupation published in the census reports for 1921, 1931, and 1951, have sought to determine what proportion of the men who reach their middle 60's in a given job are physically capable of remaining on the same job into their late 60's or beyond. They found that the proportion varied widely with the nature of the job; it was as high as 75–85% among makers of watches and clocks, workers in precious metals, and makers of musical instruments, and as low as 5–15% among coal-face workers and signalmen.

In general, it is agreed that the possession of skill offers a workman his surest prospect of employment in later life. The easiest time to acquire trade skill is at the beginning of working life, and there is still much room at that stage for enlightened vocational guidance in Britain. It is extremely difficult, especially in areas of heavy industry, for a man to acquire trade skill in later life. The tendency is all the other way, for under these circumstances even a skilled tradesman, no longer young, often finds it difficult to get back into his trade if for any reason he should fall out of employment for some time. Le Gros Clark and Dunne estimate that if their findings are true over the whole field of industry—and their study excluded unskilled labourers—about 40,000 alternative jobs would have to be found each year to save men from retiring on reaching the age of 65, and that figure would have to be increased to find jobs for those compelled to change work as a result of injury or illness. As these authors say, what we undoubtedly need is a thorough inquiry into the alternative jobs open to men who have to make a fresh start. Belbin, faced with a somewhat similar problem, suggests that the formulation of new plans and policies for training and retraining workers before they become old would represent "a most progressive and far-reaching approach" to the problem of the employment of older persons. This conception certainly represents a challenge to industrial organization. The problem is not an easy one. The industrialist may be forgiven for pointing out that retraining is an expensive business and that in some fields of labour there is little scope for it; he may even argue that the higher rates of sickness absence among older workers must make a venture into this field of doubtful economic value to the individual employer. Yet, as I. D. Grant[7] has pointed out, elderly people can be taught new tricks. The question merits serious study, for no one can rest satisfied with the present position which, in areas of predominantly heavy industry, leaves thousands of men still considerably short of pensionable age to drag out a miserable and frustrated existence in idleness on sickness or unemployment benefit, often eked out by National Assistance. Moreover, as the National Advisory Committee says in its second report,[8] published recently, there are still "many establishments and some fields of employment where the general feelings of good will towards the policy of employing the older worker need to be converted into more positive action."

CARCINOMA IN SITU

The pathological condition described as intra-epithelial carcinoma, non-invasive cancer, and carcinoma *in situ* has aroused much speculation, and R. H. Fennell and B. Castleman[1] have recently published a critical and comprehensive review of work on the subject. Unmistakable histological infiltration of surrounding tissue has long been regarded as an essential prerequisite in the histological diagnosis of cancer, but during the last few years this point of view has been changing. Lesions which to-day are considered by many to be a form of established cancer in a non-invasive stage were formerly regarded as precancerous, or possibly merely as an atypical hyperplasia, though a few precancerous lesions occurring in certain localities—for example, Bowen's disease of the skin—have long been known to be the starting point

for the development of widely invasive cancer. Now, as a result of more careful observation of both post-mortem and operation specimens, carcinomata *in situ* are known to occur in many different parts of the body, including the skin, uterus, vulva, anus, gastro-intestinal and respiratory tracts, gall-bladder, urinary system, and breast. The increasing use of cytological techniques for the identification of malignant cells in pathological fluids has been effective in detecting clinically unrecognizable cancer, and many of these lesions, especially in the cervix uteri, have proved to be examples of non-invasive carcinoma.

The macroscopic and microscopic appearances of these very early lesions vary widely in different parts of the body. In some cases little or nothing can be seen. A slightly roughened area of the squamous epithelium of the oesophagus at the level of the bifurcation of the trachea may prove to be carcinoma *in situ*. Early non-invasive carcinoma of the stomach may spread for a considerable distance within the confines of the mucous membrane with no conclusive naked-eye abnormality. Some cases of carcinoma *in situ* of the cervix uteri, first diagnosed by cytological examination of the vaginal smear, may be remarkably difficult to recognize on clinical examination. On the other hand, this early non-invasive lesion may be represented by a polyp, and association between polyps and malignant disease of the rectum is well known.

The diagnosis of carcinoma *in situ* is undoubtedly a problem for the pathologist. It depends upon the interpretation of certain histological changes in an epithelial-lined surface—namely, atypical cellular proliferation with variation in the arrangement of the cells and in their size, shape, and intensity of staining, and with mitotic figures but without invasion of the deeper tissues. These changes resemble those seen in invasive cancer and vary in degree with different grades of anaplasia. Sometimes they may be difficult to distinguish from similar appearances in young actively growing tissue or resulting from inflammation. Carcinoma *in situ* may be multifocal; it may be found in the vicinity of invasive cancer; and serial sections of some of these lesions may show histological infiltration.

Knowledge of the natural history of carcinoma *in situ* is fragmentary. Theoretically it appears feasible for all carcinomata to pass through such a stage, but the evidence for this is insufficient. The results obtained by animal experiments are conflicting. Clinically, most of the work done on the ultimate outcome of carcinoma *in situ* is concerned with lesions of the uterine cervix. There is no doubt that many of these cases progress to invasive cancer, but sometimes only after many years have elapsed. Stoddard[3] found that the interval varied from 10 months to 37 years, with an average of 9 years. The appearance of invasive cancer a short time after a diagnosis of carcinoma *in situ* has been made suggests that investigation may have been inadequate and that invasion had already taken place. During the last few years, however, a small but increasing number of patients with a diagnosis of carcinoma *in situ*, including some occurring in the cervix of pregnant women, have received no treatment, and complete regression has taken place within an observation period ranging from 5 to 15 years. There has been a tendency to discard the more radical methods of treatment and to adopt a watching attitude, with repeated biopsies, especially in younger patients.

[1] Fennell, R. H., Jr., and Castleman, B., *New Engl. J. Med.*, 1955, **252**, 985 and 1032.

[3] Stoddard, L. D., in *Progress in Fundamental Medicine*, edited by J. F. A. McManus, 1952, Philadelphia, pp. 203–260.

INITIATION OF VISUAL SENSATION

One of the most fascinating and important problems in the physiology of vision is how light energy falling on the eye is changed into a form in which it can stimulate the optic nerve. Light, as such, is known to be incapable of stimulating a nerve; it can do so only through some end-organ which is thought of as containing a photochemical substance—that is, a substance in some way affected by the light which it absorbs. Photochemical substances have been found in the rods of all vertebrate eyes that have been examined; the one which occurs in most mammals, including man, is called visual purple. When exposed to light, visual purple loses its red colour, and many workers believe that this bleaching is essential for the initiation of the nervous response and so of the light sensation. However, there is at present no firm evidence that this is so. In spite of much work on visual purple, the exact way in which it mediates the stimulation of the visual system by light remains unknown. Of great interest, therefore, is to examine other ways in which the retina can be stimulated and a sensation of light produced, for if these could be shown to act through visual purple valuable information on its mode of action might be obtained.

Recently L. E. Lipetz[1 2] has elucidated his belief that ionizing radiations stimulate the eye by virtue of a direct action on visual purple. In seeking to substantiate this hypothesis, he first made a critical study of the literature on the production of both light sensations (phosphenes) and electrical changes in the eye and optic nerve by various types of ionizing radiation. His conclusion is that the retina can be stimulated by *x* rays, gamma rays,

[1] Lipetz, L. E., *Brit. J. Ophthal.*, 1955, **39**, 577.

[2] —— *Radiation Res.*, 1955, **2**, 306.

and beta particles, and that only with the last is the stimulation due to fluorescence of the ocular media. In a further investigation Lipetz used Granit's microelectrode technique to study the impulse discharge in single retinal ganglion cells in the frog resulting from *x*-irradiation of the opened but otherwise intact eye. He found that *x* rays evoked quantitatively similar responses to those following light stimulation, that these were affected in a similar way by the state of adaptation of the eye, and that light and *x*-irradiation could to some extent replace one another. He also made some observations on the effect of *x*-irradiation on the excised, dark-adapted, unbleached retina, finding that if the intensity of radiation was high enough such retinas were bleached as they are by light. Unlike light, however, these radiations appeared to cause denaturation of the retinal proteins. He concludes that his results are consistent with, but do not prove, his hypothesis that the *x*-ray phosphene is produced by a direct action on visual purple.

Lipetz's findings may possibly not provide such good evidence for his conclusions as he claims. The inconsistencies between the effects of *x* rays and of light in producing nerve impulses seem, from his figures, to be rather serious. In addition, some of the phenomena he considers, especially the effect of adaptation to light and dark, are no longer thought to depend solely on the reactions of visual purple. Changes in the retinal neurones also play a part. Moreover, no work was done on the effect of *x* rays on solutions of visual purple, so that how these absorb very short waves is still unknown. Phosphenes and nerve impulses can also be elicited by electrical stimulation of the eye, and these reactions not only are affected by preliminary exposure to light, but also alter the responses to subsequent stimulation by light. There is no evidence that an electrical stimulus acts through visual purple, but plenty that the effect is on the retinal neurones. *X* rays and similar radiations must produce considerable ionization in the retinal tissues, as Lipetz agrees, and this will almost certainly affect the nervous structures there. More work on the reactions of visual purple to ionizing radiations would be welcome before the conclusion is reached that they act on this pigment in the same manner as light. Experiments should not be too difficult, and, if successful, might give valuable information on the way in which the properties of the visual pigments determine visual perceptions.

PULMONARY HYALINE MEMBRANE

New light has been shed on the problem of pulmonary hyaline membrane in the newborn by the work of M. J. G. Lynch and L. D. Mellor.[1 2] These authors used histochemical methods in an attempt to determine the composition and origin of the hyaline material that forms a membrane on the walls of respiratory bronchioles and alveolar ducts. The two methods used —the Lepehne–Pickworth and the "Nadi"—gave similar results, and showed that the staining reaction of the hyaline membrane was the same as that of granules in the epithelial cells lining the respiratory bronchioles. The stainable material in these cells was significantly more plentiful in lungs with hyaline membrane than in comparable controls without hyaline membrane, and among the controls it was more plentiful in the lungs of premature than of full-term infants. These observations led the authors to conclude that the hyaline membrane represents an excess of secretion from the epithelium of the respiratory bronchioles.

They do not claim to have discovered the composition of the hyaline material. Previous workers have shown that it contains polysaccharide, no serum protein, little if any mucus, and a variable and inconstant amount of stainable lipoid. The "Nadi" reaction has been said to be specific for cytochrome oxidase. Various tests applied by Lynch and Mellor indicate that an enzyme action takes place. They suggest that the secretion of the epithelium of the respiratory bronchioles may be concerned with the transference of oxygen to the blood, that oxygen may provide the stimulus necessary to produce it, and that the amount of secretion may be proportionate to the oxygen concentration. Although this theory is speculative, it offers an explanation, not provided by most of the earlier theories, of the fact that the hyaline material is never found in the lungs of infants who have survived less than one hour from birth; it also points to the possibility that administration of oxygen in high concentration may be a cause of hyaline membrane disease.

This idea is not new. It is one of several that have been advanced in recent years since the older theory of aspiration of vernix caseosa was generally discarded; but until recently it gained little support. E. L. Potter[3] considered it, but decided against it. But evidence incriminating oxygen has been accumulating. Hyaline membrane has been produced by oxygen administered in high concentration,[4] and since it has been proved to be the cause of retrolental fibroplasia it can no longer be regarded as harmless to human infants; possibly hyaline membrane is another disease for which it must be held, at least in part, responsible. An observation made by D. H. Weintraub, quoted by Lynch and Mellor, is of special interest: in his hospital in Buffalo severe curtailment of the use of oxygen was followed by a notable reduction in the incidence of hyaline membrane disease.

It has been recognized for some time that a dry atmosphere increases the risk of the formation of hyaline membrane, and high humidity is now generally maintained in the prophylaxis and treatment of the disease. This accords well with the theory advanced by Lynch and Mellor, since it is reasonable to suppose that dryness of the inspired air would cause inspissation of the secretion. These authors therefore recommend low concentration of oxygen and high humidity in the prophylaxis of hyaline membrane disease.

[1] Lynch, M. J. G., and Mellor, L. D., *Lancet*, 1955, **1**, 1002.
[2] —— —— *J. Pediat.*, 1955, **47**, 275.
[3] Potter, E. L., *Pathology of the Foetus and the Newborn*, 1952, p. 252, Chicago.
[4] Bruns, P. D., and Shields, L. V., *Amer. J. Obstet. Gynec.*, 1951, **61**, 953.

CONCEPTION DURING LACTATION

Although the common belief that pregnancy is unlikely to occur in lactating women appears to be well founded, it has not been easy to obtain reliable information about its frequency. There are two sources of difficulty: the proportion of women who feed their children for long periods is not high; and the use of other contraceptive measures makes it impossible to regard lactation as the only reason for the inhibition of conception. In a recent investigation by R. Gioiosa[1] of the histories of 500 mothers in a Catholic hospital in the United States these difficulties were largely avoided. Most of the women fed their children for many months, and the fact that a high proportion of those who were not pregnant at the end of lactation conceived soon after (more than half within four months and three-quarters within nine months) suggests that no other form of contraceptive was in common use. Forty-six of the 500 mothers, or about one in ten, became pregnant while they were still lactating. In most of these cases conception occurred after many months of breast feeding when weaning had begun; there were no conceptions in the first three months, and only 7 in the first six.

These results are consistent with other evidence that although ovarian activity is substantially reduced during lactation it is by no means completely suppressed. In more than half the cases reported by C. H. Peckham[2] and A. Sharman[3] menstruation returned before the end of lactation. T. McKeown and J. R. Gibson[4] examined the incidence of menstruation in 943 lactating women, and found that, though the cycle was fairly effectively suppressed during the early months, it reappeared in an increasing proportion of women as lactation proceeded, and returned more rapidly, even in the early months, if the child was partially weaned.

A considerable proportion of the cycles which occur during lactation are anovulatory in character, but Sharman[5] has shown that ovulation may precede the first cycle. This observation explains the occasional occurrence of a second pregnancy without reappearance of menstruation.[2 4]

From experimental and clinical evidence the influence of lactation on conception is now fairly clear. The suppression of ovarian activity is evidently due to the stimulus of suckling.[6] The suppression cannot, however, be prolonged indefinitely even when the stimulus is effectively maintained by full breast-feeding, and it becomes much less effective as soon as some form of complementary feeding is begun, presumably because the suckling stimulus is reduced. In a few women menstruation, often anovulatory,[5] proceeds throughout lactation, and the occasional occurrence of conception in the early months is usually, although not invariably, preceded by the return of the cycle.

[1] Gioiosa, R., *Amer. J. Obstet. Gynec.*, 1955, **70**, 162.
[2] Peckham, C. H., *Bull. Johns Hopk. Hosp.*, 1934, **54**, 186.
[3] Sharman, A., *J. Obstet. Gynaec. Brit. Emp.*, 1951, **58**, 440.
[4] McKeown, T., and Gibson, J. R., ibid., 1954, **61**, 824.
[5] Sharman, A., *Fertil. and Steril.*, 1951, **2**, 371.
[6] Selye, H., and McKeown, T., *Proc. Soc. exp. Biol. (N.Y.)*, 1934, **31**, 683.

MENTAL ILLNESS AND THE LAW

A White Paper[1] issued by the Department of Health for Scotland puts forward for discussion a number of proposals for changes in the Lunacy and Mental Deficiency (Scotland) Acts. Both the Scottish and English law is due for revision and consolidation, and some of the changes proposed by the Department of Health for Scotland would be equally welcome in England. Earlier this year the British Medical Association submitted a memorandum of evidence[2] to the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency, and the special committee which prepared the memorandum recommended that all adult voluntary patients should be admitted to mental hospitals without formality. When admission cannot be arranged on a voluntary basis, then, in the committee's view, admission as a "temporary patient" without a judicial order should be the normal method. A somewhat similar suggestion is made for Scotland in the White Paper just issued. If the patient is incapable of deciding whether to enter hospital as a voluntary patient, then he should be admitted as a "recommended patient," provided his relatives are willing and two medical practitioners recommend that the patient is likely to benefit from in-patient treatment. The medical superintendent of the mental hospital would have to certify to the Board of Control within fourteen days of admission that the patient suffered from mental illness and was a proper person to be detained. The same safeguards against wrong detention would apply to "recommended" patients as now apply to certified patients. The B.M.A. proposed that one of the two recommending doctors should be approved by the Board of Control, but the Scottish report makes no such stipulation. The White Paper points out that "procedure by way of judicial order will be retained as an alternative, for use when the relative is unwilling to concur in admission on the 'recommended' basis, or in other special types of case where that basis is for any reason inappropriate." The terms "lunatic," "insane person," "idiot," or "person of unsound mind," should cease to be used, and a certified patient should be detained "in order that he may be afforded the care and treatment he requires."

The B.M.A. committee recommended that the present legal distinctions between grades of mental defect should be abolished, and the White Paper takes the same view. "The certifying doctor, instead of defining by name the type of mental defect, will be required to state that the person is mentally defective, and to answer specific questions designed to ascertain what type of provision, training, and accommodation will best suit the case." In these and other ways the Scottish White Paper and the memoranda of evidence submitted to the English Royal Commission by the B.M.A., the Royal Medico-Psychological Association, and other organizations make proposals which will help to obliterate the stigma of mental disorder.

[1] "The Law Relating to Mental Illness and Mental Deficiency in Scotland: Proposals for Amendment," 1955, H.M.S.O.
[2] See *British Medical Journal Supplement*, 1955, **1**, 211.

EMERGENCIES IN GENERAL PRACTICE
CORONARY THROMBOSIS

BY

A. MORGAN JONES, M.B., M.Sc., F.R.C.P.
Director of the University Department of Cardiology, Manchester Royal Infirmary

One of the physician's principal responsibilities in this condition is to recognize when it is likely that coronary thrombosis has occurred. It is a serious mistake to believe that the onset is always marked by a dramatic attack of prolonged chest pain. Indeed, there are at least four other modes of onset: sudden onset of angina of effort; sudden exacerbation of existing angina of effort; the appearance of short attacks of cardiac pain at rest; and sudden onset of heart failure without apparent cause.

In any of these circumstances it is now commonplace to find electrocardiographic evidence of recent myocardial infarction, but if the electrocardiogram does not show any evidence of recent infarction this should not be regarded as proof of the innocence of the symptoms. The clinical assessment of the case must be made independently of the electrocardiogram. In fact, the investigation is useful only when the result is positive, and then its value probably lies as much in the handling of the patient and his relatives as in clarifying the clinical diagnosis. In the absence of a positive electrocardiogram, assessment turns principally on whether the pain is definitely cardiac. Pain at rest is clearly more difficult to assess than effort pain. Inquiry should therefore always be made for previous effort pain, for if typical angina of effort is followed by rest pain of similar character and distribution (though possibly more severe or widespread) it is very likely that the rest pain is also cardiac.

The site of cardiac pain is very variable: it may occur anywhere between the mouth and the umbilicus, anteriorly or posteriorly, or in either arm. Contrary to some published assertions, it may be confined to the left mammary region or to the back of the chest. The character is more helpful than the site, for it is usually described as tight, heavy, constricting, pressing, aching, or burning but not as stabbing or shooting. It is not usually most severe or widespread at the onset, but tends to increase in severity and to radiate to a wider area simultaneously. It more commonly starts centrally in the chest and radiates peripherally to the neck, jaw, or arms, but the reverse can occur.

Among the more important differential diagnoses are acute pericarditis, dissecting aneurysm of the aorta, pulmonary embolism, hiatus hernia, and spontaneous pneumothorax, though in my experience the last only occasionally simulates coronary thrombosis. Both acute pericarditis and massive pulmonary embolism may be associated with T-wave changes in the electrocardiogram but not with the typical pattern of infarction. The sudden onset of an arrhythmia, such as paroxysmal tachycardia, is sometimes associated with quite severe cardiac pain without myocardial infarction, but if such pain lasts more than half an hour infarction should be suspected. T-wave changes may follow a paroxysmal arrhythmia although no infarction has occurred.

Severity of the Infarction

The severity of the pain is of no significance in assessing the severity of the myocardial infarction, but intractable or recurrent pain over a period of more than forty-eight hours is, in my experience, a somewhat ominous feature. Maintenance of the blood pressure is a good sign, but an immediate considerable fall is not necessarily serious provided, as is often the case, evidence of shock is absent, for frequently there will be recovery from this early fall within twenty-four or forty-eight hours. A steady progressive fall over the first few days is more important, for in these circumstances the pressure is apt to remain low. Considerable fever and a leucocytosis of 20,000 or more are usually associated with extensive myocardial necrosis. Most of these criteria are concerned with the severity of the acute lesion, but, in fact, the prognosis really depends upon the total cardiac damage, old and recent. For this reason a history of old infarction, the presence of cardiac enlargement, and especially previous or present heart failure are important. The appearance of presystolic gallop rhythm or an attack of cardiac asthma may indicate the presence of left ventricular failure, and examination will then often reveal moist sounds at the lung bases. Right heart failure will be marked by engorged neck veins or oedema of the ankles and sacrum. Such signs are ominous.

Pericardial friction, usually present only for twenty-four to forty-eight hours, is probably an indication of a fairly large infarct, but in my experience it is not so ominous a sign as has sometimes been suggested. Cardiac arrhythmias, such as auricular flutter or fibrillation, and ventricular paroxysmal tachycardia are serious and require prompt treatment, but occasional premature beats are exceedingly common and not often followed by more serious arrhythmias; so they are probably better left untreated to disappear spontaneously in a few days. Very frequent ventricular premature beats have greater significance.

Management of the Acute Attack

The objects of immediate treatment are to allay anxiety, to relieve pain, to treat shock or heart failure, and to control serious arrhythmias. Nothing which the physician can say will allay anxiety so effectively as an unruffled and matter-of-fact approach to the patient, and if the doctor is sometimes himself anxious it is worth remembering that recovery is the rule if the patient is still alive when he arrives. The relief of pain is of immediate importance. It is traditional to give large doses of morphine, usually ½ gr. (32 mg.). I doubt if it is desirable, however, to give repeated large doses of morphine in an attempt to remove all pain, for although this may induce sleep, complete relief of pain without unconsciousness is not, in my experience, attainable except by natural remission. Furthermore, very large and especially repeated morphine injections may lead to vomiting and later to troublesome constipation and lack of appetite. I therefore prefer the minimum dose which will make the pain tolerable, rather than rigid adherence to the large doses traditionally recommended in textbooks. If morphine in moderate doses does not make the pain tolerable, oxygen, preferably by tent, will sometimes help. Once the pain has eased, it is better to avoid morphine altogether.

There is no really satisfactory treatment for shock due to extensive myocardial damage, and most of the measures suggested, such as 50% glucose intravenously or small transfusions, are positively dangerous because they may precipitate acute heart failure. The best plan is to leave the patient where he is and keep him reasonably warm, but not to heap blankets upon him to near suffocation. If severe hypotension (80 mm. Hg) develops it may be lifesaving to raise the blood pressure to 100–110 mm. Hg

by a noradrenaline drip (1:10,000), for this will maintain the myocardial and renal circulations. This technique requires very careful observation, for the blood pressure can be varied almost instantaneously by altering the drip rate, and readings must therefore be taken every fifteen minutes and the rate varied correspondingly.

Treatment of acute left heart failure with pulmonary oedema follows the usual lines, but I would like to emphasize the value of the slow intravenous injection of 0.5 g. of aminophylline in 20 ml. of solution.

Arrhythmias such as auricular flutter and fibrillation are treated by the usual methods, but the most rapid method of control should be chosen—that is, by intravenous digoxin.

Admission to Hospital

It is very doubtful whether any community will in the future be able to provide enough hospital beds for the treatment of all cases of coronary thrombosis, even if this were desirable. In my view, cases in which anticoagulant therapy is to be used should be admitted to hospital at the present time, for at home satisfactory laboratory control of this treatment is exceedingly difficult, though perhaps not impossible. In general, therefore, the present criterion for hospital admission is the desirability of anticoagulant treatment.

So far there is no uniformity of opinion about the desirability of anticoagulants, for all shades of opinion exist in this country from that of William Evans—"That anticoagulant treatment of coronary occlusion will go the way of other discarded remedies is certain. Let it go now"—to that of Rae Gilchrist—"Anticoagulants are justified by a halving of the death rate and by an even greater reduction in thrombo-embolic episodes." In controlled series published throughout the world the mortality in cases treated with anticoagulants has averaged 16.6% in 1,091 cases, whereas in the corresponding control series treated by conservative methods the mortality averaged 32.4% in 1,344 cases. If, however, we separate off what are termed "good risk" cases we get a somewhat different picture. A patient with recent coronary thrombosis is generally regarded as a "good risk" if there has been no previous infarction, if there is no intractable pain, no severe shock, and no cardiac enlargement, gallop rhythm, heart failure, or significant arrhythmia. In addition there should be no indication of a liability to thrombo-embolism, such as varicose veins in the legs or a previous history of thrombophlebitis or pulmonary embolism.

These criteria may appear to eliminate a large proportion of cases, but in fact they do allow about half the cases to be regarded as "good risks." In 489 such cases recently reviewed the mortality was only 3.1% and the reduction of mortality by anticoagulants only 1%. In such cases the gain from the use of anticoagulants is relatively small and against that gain must be set the risk of transport to hospital and the risk of anticoagulant therapy. It is true, of course, that a "good risk" case at the outset may, owing to further infarction, become a "bad risk" case. These patients include, of course, the 3% who die. It has often been held that uncertainty of the outcome is one of the outstanding clinical features of coronary thrombosis, but there must be few serious conditions in which we can at the onset separate off clinically so large a proportion of cases with so hopeful and encouraging a prognosis. My experience has certainly been in conformity with this view, and my own practice is, after careful assessment, to encourage the treatment of "good risk" cases at home by conservative methods. In the "bad risk" case, on the other hand, I very strongly advise anticoagulant treatment in hospital, for I believe that in these cases all the available evidence indicates that anticoagulants substantially reduce the mortality.

Control of Anticoagulant Therapy

Anticoagulant treatment can be controlled *only* by regular estimation of prothrombin activity in the blood, and this is usually necessary daily at first. Even if a patient's anticoagulant requirement is known on one occasion it may be quite different in a subsequent illness. The institution of anticoagulant therapy should therefore always be undertaken in hospital unless reliable daily laboratory facilities are available at home. Once it has been shown that the patient's requirement of anticoagulants is steady, continuation may be possible at home with weekly or twice weekly prothrombin estimations.

In my department anticoagulant treatment in coronary thrombosis follows the same general lines as those laid down by Rob for peripheral arterial occlusion in his article earlier in this series,* but heparin is used at the onset only if there is initial shock. Prothrombin activity is estimated on admission and a low initial reading is regarded as an indication of liver damage; if below 50% anticoagulants should not be given, and if between 50 and 75% caution is necessary. A history of recent spontaneous bleeding (for instance, from a peptic ulcer) is a contraindication. The initial dose of phenindione is 200 mg. by mouth if the preliminary prothrombin level is normal. All subsequent doses are controlled entirely by the prothrombin level, which should be reduced to 20%. The stabilized daily requirement varies from 25 to 250 mg. and may fluctuate from time to time. For subsequent out-patient treatment it is therefore safer to aim at a level of 30%. In the early days of anticoagulants spontaneous and sometimes fatal bleeding from bowel, kidneys, or into the tissues often occurred, but with careful control haemorrhage is now very uncommon and almost never fatal. The most effective antidote is vitamin K_1 orally (20 mg.), but this is still difficult to obtain, and injected "synkavit" (50–100 mg.) is useful but less effective. Anticoagulants once started should be continued until the patient is up for part of the day.

General Management

The following observations apply whether the patient is treated conservatively at home or with anticoagulants in hospital.

Reassurance.—Once a patient knows he has had a coronary thrombosis—and this cannot usually be concealed from him—anxieties crowd upon him. His heart, to which he may never have given a thought, has let him down, and this is, in the popular view, the vital organ; he fears, first, that he may lose his life; then that he may be permanently crippled; and, finally, although he may survive free from symptoms, he fears a recurrence. He may say little of these fears, yet he wants them allayed. In my view it is his physician's duty to reassure him, and in great part this is medically justified. The majority do survive and return to a normal, if slightly less hectic, life; if the condition recurs, it may not do so for very many years, and he may again make as good a recovery as before. Older views on prognosis are unjustifiably gloomy. The technique of reassurance is important, for exaggerated or over-dogmatic statements will be discounted by an intelligent patient. His confidence will lie in the physician who himself believes and acts and talks at all times with a quiet confidence in ultimate recovery; who assumes that, after a space of time for complete healing, resumption of a normal life is the rule. In this atmosphere those who recover will do so with patience and determination, and without unnecessary uncertainty and fear.

Rest.—Rest for four to six weeks is still generally regarded as desirable in coronary thrombosis, but the days of rest flat in bed—rigidly immobile, being fed, and being uncomfortably balanced on bedpans—are, if not gone, at least, I hope, numbered. If this spirit of tense apprehension dominates the sickroom the patient's future may well look as blank to him as the ceiling which is made to form almost the whole of his field of vision. We know, both from clinical experience and from scientific measurement, that the

*"Sudden Occlusion of a Major Peripheral Artery," by Professor C. G. Rob (*Journal*, February 12, 1955, p. 407).

physical effort of using a commode is much less than that of maintaining a precarious balance upon an apparently razor-edged bedpan which tilts unpredictably upon a yielding mattress. Rigid immobility in bed predisposes to thrombo-embolism, as does over-sedation. In the more severe cases, and especially those with shock, the patient may be fed and shaved for the first week, but whatever level of rest is imposed at first it should be progressively, though gradually, relaxed so that each week the patient feels that he is making some progress. In the last (fourth to sixth) week before the patient gets out of bed, breathing and leg exercises will help to restore his flabby muscles and build up his morale. In old people some period out of bed in a comfortable chair may well be instituted from the end of the first week. The keynote of the management of activity is gradual increase from the end of the initial phase of shock (if present), lack of appetite, and general malaise, which usually lasts only a few days. After that time most patients feel so well that it is necessary to explain to them the need for a sufficient period of comparative rest to ensure sound healing.

Drugs.—Apart from a gentle sedative during the day and perhaps a soporific at night, anticoagulants are generally the only medicinal treatment necessary. Too much attention to the bowels is to be discouraged in the first week, for a few days of "constipation" are physiological following the days at the onset when little food is desired.

Heart Failure.—Constant watch should be kept for early signs of heart failure, especially sacral oedema, cervical venous engorgement, a tendency to breathlessness in bed, and basal pulmonary congestion. The legs should be examined regularly for oedema or thrombophlebitis. Treatment for early heart failure, if necessary, follows the usual lines. If there is any tendency to heart failure the patient should be nursed sitting—oedema in the lower back or ankles never killed anyone, but fluid in the lungs is much more dangerous. For nocturnal breathlessness, associated with early left ventricular failure, "nepenthe"—30 min. (1.7 ml.)—at night is often an effective immediate prophylactic, but treatment should be by mercurial diuretics and salt restriction.

Visitors.—Some limitation is desirable in the first three weeks, and generally this can be effected only by confining the privilege to the family. But if a single urgent business matter needs attention, it is better to allow a visit for this purpose rather than permit the patient to worry about it. After the third week a telephone may be made available and short visits from friends encouraged.

Diet.—Light, small meals should be the rule, and this is especially true if the patient is overweight, but in any case there is a tendency to gain weight in bed and this should be guarded against. From the third week the patient should be weighed weekly at the bedside.

Tobacco and Alcohol.—Although there is no satisfactory evidence that tobacco is harmful in coronary thrombosis, it is probably wiser to prohibit it during the first two weeks and then, if the patient clearly feels the need for it, to allow not more than ten cigarettes a day. There is no contra-indication to the moderate use of alcohol, except that allowance must be made for the additional calorie intake.

Details of management can be described without end, but all decisions finally depend upon a common-sense approach which recognizes the patient's need for outward signs of steady progress and his dependence upon a background of quiet confidence.

Extension of Infarction

It is my practice to have a weekly electrocardiogram, for if a recent reading is available for comparison this assists in the interpretation of any recurrence of cardiac pain. The degree of change in serial records, however, has never seemed to me to bear much relation to the clinical progress of the patient. Pathological evidence from our recent studies indicates that extension of an infarct is usually due to necrosis of ischaemic muscle related to the original occlusion and not due to fresh coronary occlusion. This tendency for extension exists for about four weeks, and since it does not imply a new coronary thrombosis I doubt if it should be allowed to increase the period of rest very much.

Convalescence and Subsequent Life

If the management of the period of bed rest has been psychologically sound the patient should come to the time of ambulation with an expectation of ultimate satisfactory recovery, but a realization that this will take some weeks or months. He will not expect to get up and go about his business, for he will know that owing to the period of bed rest his muscles will be flabby and will require progressive use to recover, and he will have been warned that some two months must elapse before the final stages of cardiac healing are complete and he can resume his life in a more or less ordinary way. Although the pace at which convalescence proceeds may be modified by the total cardiac damage and the temperament (either apprehensive or optimistic) of the patient, it is a good general rule to prescribe a month of gradually increasing activity at home followed by a quiet holiday of three or four weeks in a flat place. It is only during the first week at home that stairs need be avoided, provided they are taken quietly. A month after he returns home he should be able to drive his car locally, but not on long journeys. Abstinence from sexual intercourse during the period of convalescence of three to six months is probably advisable.

In the majority of cases in which heart failure has not occurred the patient will be able to resume the sort of life he has led before, provided this was a reasonable one. He will need only to avoid excesses of any kind: smoking, drinking, eating, work, idleness, worry, long hours, etc. If he drives a car for long distances, he should do so in easy stages. The golden rule for him is to allow plenty of time for anything he does, from catching a train to eating a meal. But a coddled and cosseted life of inactivity is as bad, or worse, than too busy a life, with snatched meals and hardly caught trains. In fact, he should lead the sort of life we all ought to lead—in full health we may escape retribution if we ignore the rules of a sensible life, but we cannot afford this indulgence after a coronary thrombosis.

Except for the heaviest manual job and work involving responsibility for the lives of others—for example, bus-drivers, engine-drivers, aircraft pilots—there are few occupations which a man is justified in leaving because he has had a coronary thrombosis, provided this has not been accompanied by heart failure. But he may have to plan his work more efficiently, especially if it is largely administrative, and learn to depute responsibility. Amongst manual workers, experience shows that, in the coronary age group, attempts to move men to lighter occupations often fail because they either return to their old work or give up altogether.

Conclusion

Finally, all that I have seen of coronary disease has convinced me that the management of the patient is even more important than the treatment of the disease: there is often far more residual disability from fear than from myocardial damage—and it is largely within our power to prevent this.

Next article on Emergencies in General Practice.—"Birth Trauma," by Dr. A. P. Norman.

Refresher Course Book.—Copies of the second volume of collected articles from the Refresher Course for General Practitioners are still available at 25s. (postage—inland 1s. 6d., overseas 1s.) each from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller. The first volume is now sold out.

THE HEBERDEN SOCIETY

The annual meeting of the Heberden Society was held in London on November 25 and 26, under the chairmanship of the president, Professor R. E. TUNBRIDGE. Seven papers were read.

Spondylitis and Heart Disease

Dr. J. SHARP (Manchester University) found that 25 out of a group of 788 patients attending a spondylitis clinic had disease of the mitral or aortic heart valves. Three of them, all with pure aortic disease, appeared to be suffering from typical ankylosing spondylitis, and it was suggested that the processes in the spine and heart might be related. In at least seven others the changes in the heart, spine, and sacro-iliac and limb joints appeared to have resulted from severe attacks of rheumatic fever. The clinical features of these 7 and of 12 further patients, apparently suffering from the same condition but who had not been referred to the spondylitis clinic, were described. Seventeen of them had varying degrees of permanent change in the limb joints of the type originally described by Jaccoud, and 12 had residual limitation of spinal movement. Radiographically the sacro-iliac joints were frequently involved. The changes in the spine were characterized by alteration in shape and sometimes hypoplasia of the vertebral bodies, narrowing and ossification of multiple disks without vertebral osteophytosis, apophyseal joint involvement progressing to bony ankylosis, and, occasionally, ossification of spinal ligaments. In its complete form this radiographic picture was recognizably different from that of typical ankylosing spondylitis.

Deep *x*-ray therapy did not appear to be of value in such patients, but they were usually greatly helped by aspirin. The most important measures in their long-term management appeared to be the prevention and early treatment of streptococcal infections.

Prednisone and Prednisolone

Dr. H. F. WEST (Sheffield) opened a discussion on two new steroids, prednisone (Δ^1dehydrocortisone) and prednisolone (Δ^1dehydro-hydrocortisone).* The ability of prednisone to produce suppression of the adrenal gland was approximately the same as that of a dose of hydrocortisone equal in therapeutic potency. Dr. O. SAVAGE confirmed the therapeutic effectiveness of the new substances—particularly evident in an improvement in strength of grip. In different patients they had proved to be from two to ten times as potent as cortisone. Dyspepsia was a common toxic effect, but was not invariably worse with the new steroids than with cortisone. Cases of afebrile pneumonia and staphylococcal septicaemia had occurred during treatment. Dr. M. THOMPSON said that in the United States haemorrhage from the upper or lower alimentary tract was a recognized danger of treatment with the new steroids. After several months of treatment the dose often had to be increased to maintain suppression of the disease, but a change to cortisone was sometimes an effective alternative to this. Dr. G. D. KERSLEY had found prednisolone useful in treating a case of rheumatoid arthritis with heart failure and oedema. Dr. F. DUDLEY HART had been impressed by the promptness of the response to the new steroids. He felt, however, that the increased incidence of dyspepsia associated with their use outweighed the advantage of their negligible effect on sodium metabolism. Dr. A. ST. J. DIXON commented on the "lift" which a patient experienced when he was transferred from cortisone to one of the new compounds. Dr. E. G. L. BYWATERS stressed that the incidence of side-effects was the crux of the problem, and that it was too early to draw firm conclusions on this. Dr. J. J. R. DUTHIE was anxious about the effect on the integrity of joints of completely suppressing inflammation and thereby removing a check to their over-use.

Rheumatoid Arthritis in a Sample Population

Professor J. H. KELLGREN (Manchester University) described a survey in which a sample of the general population aged 55–64 years was examined clinically, radiologically, and serologically for evidence of rheumatoid arthritis. Clinical evidence of rheumatoid arthritis was found twice as frequently in women as in men, but *x*-ray signs of rheumatoid arthritis and positive sheep-cell agglutination tests were equally distributed between the sexes. In 9 out of 10 individuals with severe clinical rheumatoid arthritis the diagnosis was confirmed by the *x*-ray appearance and/or a positive agglutination test, but with lesser degrees of clinical disease such confirmation was less usual. Among the 283 individuals who had been recorded as being free from clinical evidence of rheumatoid arthritis 20 had positive radiographs and/or agglutination tests. The prevalence rates in this sample ranged from 1% for men and 3% for women for severe clinical rheumatoid arthritis to 11% for men and 27% for women if all grades of clinical disease, including a past history of polyarthritis, were counted. Thus precise diagnostic definition was essential if prevalence rates in different populations were to be compared.

Osteoarthritis in the Same Population

Dr. J. S. LAWRENCE (Manchester University) had found radiological osteoarthritis in 83% of the males and 87% of the females between the ages of 55 and 64 from the same sample. The condition was multiple (more than four groups of joints affected) in 39% of males and 49% of females. Females had significantly more radiological osteoarthritis in the distal and proximal interphalangeal joints of the fingers, in the carpo-metacarpal joints, in the knees, and in the metatarso-phalangeal joints of the feet. Males had significantly more osteoarthritis only in the wrists.

Two main factors appeared to be responsible for the greater prevalence of multiple osteoarthritis in females. (1) A factor, believed to be genetic, associated with clinical Heberden's nodes and with osteoarthritis of the interphalangeal, metacarpo-phalangeal, and carpo-metacarpal joints of the hands, the interfacetal joints of the cervical spine, the sacro-iliac joints, and the metatarso-phalangeal joints of the feet; (2) a second factor, possibly also genetic, and associated with obesity and with osteoarthritis of only the weight-bearing joints. Other causative factors—trauma, deformities, occupation, and rheumatoid arthritis played a relatively minor part in determining the osteoarthritic joint pattern in females.

Arthritis Associated with Psoriasis

Dr. V. WRIGHT (Stoke Mandeville) described clinical and laboratory findings in 31 cases of arthritis associated with psoriasis. In 25 patients the arthritis was of atrophic type, five had degenerative joint disease, and one rheumatic fever. Lesions in the skin most commonly antedated the arthritis, but changes in the nails came on at the same time as the joint lesions much more often and tended to wax and wane in parallel with the arthritis. At its onset the arthritis was less often polyarticular than in classical rheumatoid arthritis. Although the distal interphalangeal joints were most commonly the first joints to be involved, the process did not remain confined to them, and there seemed no reason to distinguish psoriatic arthropathy as a clinical entity in which only these joints were affected. Other clinical features of atrophic arthritis associated with psoriasis were a tendency to mimic gout, a high incidence of very complete remissions, prominence of morning stiffness in the symptomatology, and a tendency for the disease to be either very severe or very mild. Among the five cases with osteoarthritis there were, rather surprisingly, four with changes in the nails.

The meeting concluded with papers by Dr. D. S. JACKSON (Manchester University) on a new method of isolating and purifying the so-called "alkali-soluble collagen," and by Drs. I. GILLILAND, I. ISDALE, and E. M. ABDEL-WAHAB (Postgraduate Medical School of London) on changes in the serum proteins during the course of an attack of rheumatic fever.

British Medical Journal*, 1955, **1, 1520.

Preparations and Appliances

A SIMPLE SPLINT FOR EARLY HAMMER-TOE AND CLAW-TOE DEFORMITY

Mr. J. H. S. SCOTT, resident surgical officer, Wingfield-Morris Orthopaedic Hospital, writes : The splint illustrated below has been found useful in relieving symptoms and controlling hammer-toe and claw-toe deformity which is mobile. A comfortable and efficient splint can be made with needle, thread, and some garter elastic. The splint consists of a loop of white garter elastic ½ in. (1.3 cm.) broad, twisted twice upon itself before being stitched. This forms the garter into a figure-of-8 (Fig. 1). One portion of the "eight" encircles the affected toe and the other the heel, the intervening portion crossing under the sole of the foot (Figs. 2 and 3). The total length of the garter should be two-thirds of the measured distance round the toe and heel. This difference in length produces enough tension to flex the metatarso-phalangeal joint. Counter-pressure from below by the shoe extends the toe at the interphalangeal joints, reproducing the action of the intrinsic muscles.

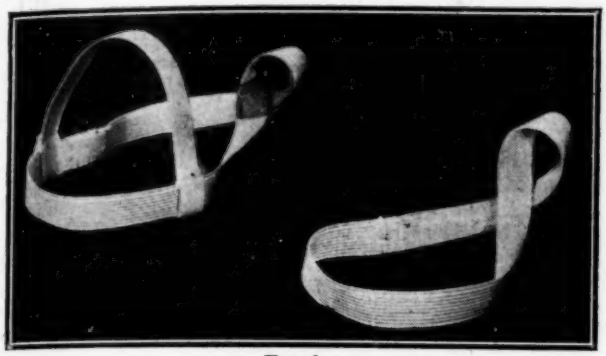


FIG. 1

FIG. 2

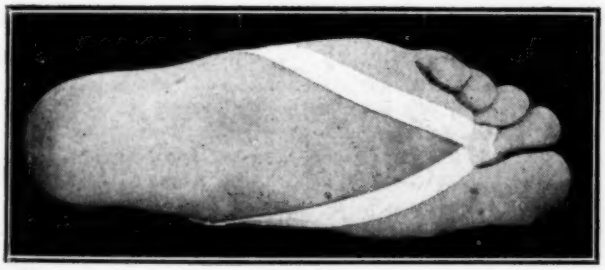


FIG. 3

This simple garter is improved by the modifications devised by Mr. Baker, superintendent of the Wingfield-Morris Orthopaedic Hospital Workshops. The toe loop is stitched and lined with soft chamois leather. A loop, passing over the dorsum of the foot, prevents the garter slipping off the heel. This loop should not be stitched to the garter but pass round it at each end and be stitched to itself so that it can be moved. The stitching of the garter itself should be placed to avoid pressure on the heel (Fig. 1).

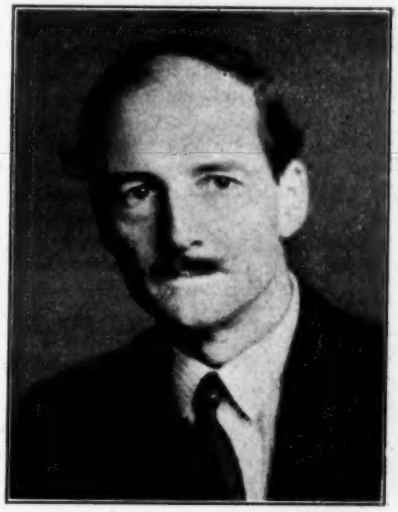
We thank Mrs. Phyllis Lorton, of Oxford, who devised the original garter.

NEW MINISTER OF HEALTH

MR. R. H. TURTON APPOINTED

On December 20 the PRIME MINISTER announced the appointment of Mr. R. H. TURTON as Minister of Health in place of Mr. IAIN MACLEOD, who becomes Minister of Labour with a seat in the Cabinet. Mr. Macleod was appointed Minister of Health in May, 1952. Mr. Turton has held office as Joint Under-Secretary for Foreign Affairs since 1954. The present changes are part of a large Ministerial reshuffle.

Mr. Turton was born in 1903 and educated at Eton and Oxford. On going down from Oxford he was for a time resident at Toynbee Hall, where he helped to run the Whitechapel Poor Man's Lawyer at a boys' and men's club in Limehouse. In 1926 he was called to the Bar by the Inner Temple, and until 1935 he practised on the North-eastern Circuit. Since that date he has been a justice of the peace for the North Riding. A territorial officer in the Green Howards during the second world war, Mr. Turton served in France, Cyprus, Iraq, Lebanon, and the Western Desert. He was adjutant of the 4th Battalion in France, and later staff captain on Lord Gort's H.Q., D.A.A.G. of the 50th Northumbrian Division, and A.A.G. Liaison on H.Q., Middle East Forces. He was awarded the M.C. at Gazala.



[*Walter Stoneman*

On his uncle's death in 1929 Mr. Turton succeeded him as Member of Parliament for the Thirsk and Malton Division (Yorkshire), which he has represented ever since.

Mr. Turton was appointed Parliamentary Secretary to the Ministry of National Insurance after the General Election of October, 1951. On the merging of that Ministry with the Ministry of Pensions in September, 1953, he became Joint Parliamentary Secretary. In October, 1954, he was appointed Parliamentary Under-Secretary for Foreign Affairs. He has been responsible for two Acts of Parliament. In 1929–30 he introduced and carried into law the Poor Prisoners' Defence Act, 1930, and in 1933 he was similarly successful with the Summary Jurisdiction (Appeal) Act. By these two measures an accused man without means has the opportunity of having his case properly presented in court. Mr. Turton was secretary of the 1922 Committee in the 1935 Parliament and vice-chairman of the committee in 1949 and 1950. He filled the offices of secretary and treasurer of the Conservative Agricultural Committee at various periods between 1935 and 1950, and was chairman of the Conservative Africa Committee in the 1945 Parliament.

Mr. Turton farms 500 acres near Thirsk, where he has a pedigree herd of Shorthorn cattle. He married in 1928, and has three sons and one daughter.

Correspondence

Radioactive Iodine for Toxic Goitre

SIR,—In your interesting leading article on the treatment of toxic goitre (*Journal*, November 19, p. 1260) you compare the techniques applied by our group in Sheffield (G. W. Blomfield *et al.*, p. 1223) with those of Russell Fraser and his colleagues in Hammersmith.[1] You remark that the routine use by the latter group of antithyroid drugs as a preliminary preparation for radio-iodine therapy makes the distribution of the isotope more uniform, and "moreover, a smaller dose of radio-iodine is required." There is no doubt that such preliminary drug treatment has many advantages, as a euthyroid rather than a thyrotoxic patient is subjected to isotope therapy, and, in particular, the incidence of myxoedema following such therapy would appear to be appreciably less than that encountered by our method. These results are, however, achieved by the use of much larger, not smaller, doses of radio-iodine than we have found to be necessary. A comparison of the published results[1] and of the results communicated to the Association of Physicians in 1953[2] shows that the drug-treated thyroid glands receive about 25–30% more radiation than the unprepared glands, and the therapeutic drinks of radio-iodine given to such patients are consequently larger. This suggests that, as we remarked in our paper, the preliminary treatment with antithyroid drugs bestows a degree of radio-resistance upon the untreated thyrotoxic gland, necessitating higher doses of radiation to achieve satisfactory clinical results.—We are, etc.,

Edinburgh. A. G. MACGREGOR.
Glasgow. E. J. WAYNE.

REFERENCES

1 Fraser, R., Abbatt, J. D., and Stewart, F. S., *Brit. J. Radiol.*, 1954, **27**, 23.
2 —— —— *Quart. J. Med.*, 1953, **22**, 509.

SIR,—I have just seen the paper by Dr. G. W. Blomfield and his colleagues (*Journal*, November 19, p. 1223). They comment on the absence of evidence that thyroid radiation is carcinogenic in man. In a recent paper[1] we reported a study of children who received radiation to the thymus gland in infancy and noted the unusually high incidence of thyroid carcinoma and adenoma during later childhood and adolescence. Further analysis of the data has convinced me that this is a radiation effect. D. E. Clark[2] was able to trace a history of radiation in all of his thirteen cases of thyroid cancer in childhood and adolescence.

I have also seen several cases apparently following radiation to the neck region in later childhood, although I have not found this history in every case. A surprising observation in both these studies is that the total skin dose given was in general in the range of 250–700 roentgens, very much lower than that generally recognized to be carcinogenic.—I am, etc.,

Buffalo, N.Y. C. LENORE SIMPSON.

REFERENCES

1 Simpson, C. L., Hempelmann, L. H., and Fuller, L. M., *Radiology*, 1955, **64**, 840.
2 Clark, D. E., *J. Amer. med. Ass.*, 1950, **159**, 1007.

Carotid Sinus Syndrome Due to Hypersensitive Carotid Sinus

SIR,—This syndrome was probably first described as a clinical entity in 1933 by Weiss and Baker.[1] Further papers by Weiss and his associates have dealt fully with the clinical features of the subject.[2 3] It has been found at times to be associated with, and due to, a carotid body tumour.[4] In some people, however, whose carotid sinus is hypersensitive, these attacks can be brought on by stimulation. The following is such a case.

A man, aged 45, who otherwise was perfectly healthy, complained of attacks of dizziness and, when standing, unsteadiness of gait. This was associated with sweating, a sinking sensation in the hypogastrium, nausea, and occasional vomiting. These attacks were occurring quite regularly, as a result of which he was off work frequently. Following such an attack he was admitted to hospital and underwent full investigations, all of which proved negative. While in the hospital under observation he did not have any attacks. After his discharge from hospital the attacks recurred, and the patient became unhappily convinced that he was suffering from a serious heart complaint. He was seen again in domiciliary consultation, and it was brought to light that these attacks usually occurred when he was wearing a stiff collar and that sudden stretching movements of the head brought them on. He also volunteered the information that the attacks had occurred when lying on his right side on the settee.

A diagnosis of carotid sinus syndrome suggested itself, and in fact a complete attack was reproduced experimentally by digital pressure on the right carotid sinus. Within a few seconds of the pressure being applied there was an increase in the rate and depth of respiration, the blood pressure and the heart rate fell, the patient started sweating and experienced nausea. On release of the pressure there was a quick return to normal. Pressure on the left sinus did not produce any symptoms. The condition was explained to the patient and he was reassured as to there being no heart disease whatever; he was advised to wear soft collars a size larger than usual, and since following this advice he has been quite happy and has had no further attacks.

Two further points are worthy of mention. First, that during his week of observation in hospital he was in bed the whole time and wearing pyjamas, and therefore there was no possibility of sinus syncope occurring. Secondly, on going back into his history he mentioned that years ago, when serving in the Guards, he frequently used to faint when on parade in full uniform, which included buttoned-up stiff collars, and one wonders, when hearing of Guards who faint when in full dress on parade, how often this is in fact due to carotid sinus syncope and not merely to fatigue, as is so often assumed.

I am indebted to Dr. I. Ansell for his help with this case.—I am, etc.,

Liverpool, 11. E. ROGANS.

REFERENCES

1 Weiss, S., and Baker, J. P., *Medicine (Baltimore)*, 1953, **12**, 297.
2 Ferris, E. B., Capps, R. B., and Weiss, S., ibid., 1935, **14**, 377.
3 Weiss, S., Capps, R. B., Ferris, E. B., and Munro, D., *Arch. Intern. Med.*, 1936, **58**, 407.
4 Michie, W., and Simpson, R. G., *Edinb. med. J.*, 1952, **59**, 443.

Inadequate Treatment of Early Syphilis

SIR,—In his memorandum on the effects of inadequately treated early syphilis Dr. F. Lanceley (*Journal*, November 5, p. 1127) does well to draw attention to the dangers of indiscriminate penicillin therapy. A patient with specific sixth-nerve palsy who came under our care recently had four daily injections of penicillin in 1948 for an eruption which had appeared on the penis soon after promiscuous intercourse. As in Dr. Lanceley's second case, this treatment was given in a casualty department without any attempt being made to diagnose the condition.

It is hoped that Dr. Lanceley's warning that early syphilis has not yet disappeared will be heeded, and that the indiscriminate use of penicillin in genital infections will be discontinued. Infective lesions of the genitals seen in this country rarely require urgent treatment, and usually indeed this can safely be withheld until investigations have been carried out. Also we would point out that penicillin is seldom indicated and frequently of little value in such infections when these are of non-specific origin.—We are, etc.,

GERALD H. KNIGHT.
Birmingham, 4. W. FOWLER.

Forty Years On

SIR,—All I have in common with Dr. A. H. Morley (*Journal*, December 3, p. 1351) is forty years' experience, and as a manufacturing chemist my observations on the development of medicine are from a different angle. No one can dispute the importance of diagnosis, but his vehement dislike of new remedies is surprising. Where would

medicine be to-day without "the innumerable drugs which pour from analytical laboratories"? Granted that some of them may not justify their existence for long, but without trials it would be impossible to ascertain their therapeutic values. The practitioner should (and indeed does) welcome information about new medicines and there is little evidence that he is embarrassed by it. Certainly no doctor is expected to "inflict on his patients every new drug as it arrives."

It is usual for manufacturers to supply proofs of therapeutic efficacy in the form of results of clinical investigations, and it is for the practitioner, according to his own judgment and individual experience, to decide what to include in his armamentarium. If Dr. Morley has paid regard to the "wise teacher" who advised him to be two or three years behind the times, then it seems that many of his patients waited unduly long for the benefits bestowed by the introduction of liver extracts, insulin, penicillin, and sulphonamides which he himself quotes. These, and hundreds of useful preparations, although not always of the same revolutionary kind, may never have seen the light of day had doctors adopted the attitude of wait and see what the other fellow will be doing.

Persons better qualified than I will probably argue the value Dr. Morley puts on old-fashioned remedies as compared with new, but few will doubt that the interests of medical progress are well served by co-operation between doctors, in hospital and private practice, and the pharmaceutical industry. He appears to be a great admirer of Sir Robert Hutchison. May I therefore remind him of what Sir Robert wrote in his *Index of Treatment*[1] (1940, p. 2): "It is usually wise to be a *little* [my italics] behind the fashion in matters of treatment; but whilst conservative, one should also be ready to accept methods of proved efficacy, no matter whence they come. Do not say, like Caiaphas, 'This man speaketh blasphemy.'"

And the good advice of Pope[2]:

> "Be not the first by whom the new is tried,
> Nor yet the last to lay the old aside."

—I am, etc.,

S. BROOK,
Managing Director,
Westminster Laboratories, Ltd.

London, N.W.1.

REFERENCES

1 Hutchison, R., *Index of Treatment*, 1940, p. 2. Bristol.
2 Pope, Alexander, *Essay on Criticism*, part 2, line 133.

SIR,—I found the article by Dr. A. H. Morley, "Forty Years On" (*Journal*, December 3, p. 1351), most stimulating and interesting.

Three or four years ago there occurred in my practice two cases of tetanus, both in children, and one of the children died. I approached a well-known ethical drug house and suggested that it would be a good idea to bring in a triple antigen to prevent such cases, and also to prevent the dilemma of whether to use anti-tetanus serum. I commenced to use "triple antigen" as soon as it was available.

A boy born on August 9, 1954, was immunized with triple antigen at monthly intervals, commencing on July 15, 1955. He was bitten on the finger quite severely by a dog on December 7, 1955, and he was the first case where I have had cause to be grateful for the use of triple antigen. I am sure there will be many more to follow.—I am, etc.,

T. DAVID LAMBERT.

Ruislip, Middx.

Treatment of Centipede Bites

SIR,—Centipedes (*Myriopoda*) are the only poisonous animals here, and the standard treatment according to my textbooks[1 2] is ammonia locally, sedatives for the pain—sometimes morphine being necessary. The species here reaches 10 in. (25 cm.) in length.

I have found the injection of "xylotox" 2% with epinephrine to provide instantaneous relief of pain, and in case this has not been mentioned before, or is not generally known, I wonder if you think the treatment worth publishing. Infection locally is not uncommon as a complication, so my routine includes anti-tetanic serum and procaine penicillin 600,000 units. I have never found it necessary to hospitalize for 2–5 days, as one writer mentions. The swelling of a ring finger may be so great as to necessitate the removal of the ring, as the blood supply to the finger becomes jeopardized. Some immunity follows the first bite, as subsequent bites are not so painful or distressing.—I am, etc.,

E. R. BLAY.

Christmas Island.

REFERENCES

1 Manson-Bahr, P. H., *Tropical Diseases*, 1954. London.
2 Mackie, T. T., Hunter, G. W., and Worth, C. B., *Manual of Tropical Medicine*, 1954. Philadelphia.

Treatment of Simple Rib Fractures

SIR,—Suggesting long-lasting local analgesia in treatment of broken ribs, Mr. H. D. W. Powell (*Journal*, October 1, p. 829) mentions benzocaine-urethane solution as advocated by Rutter.[1] There is no reference to the previous work of F. Rappaport,[2] who described this solution as long ago as 1946, and of E. Spiro,[3] who was the first to apply it clinically. Rutter has cited these original authors in his letter on relief of post-operative pain,[1] and so have Kohn and Vitali.[4]

As the subject of prolonged analgesia is again and again treated in a number of papers, and to enable prospective authors to relate all the previous work performed on this topic, I beg to draw your attention to the above-mentioned facts.—I am, etc.,

Z. RIX.

Jerusalem.

REFERENCES

1 Rutter, A. G., *British Medical Journal*, 1952, 2, 1418.
2 Rappaport, F., *Acta med. orient. (Tel-Aviv)*, 1946, 5, 115.
3 Spiro, E., ibid., 1946, 5, 119.
4 Kohn, J., and Vitali, M., *Lancet*, 1953, 1, 1312.

Dimenhydrinate for Vomiting During Pneumoencephalography

SIR,—During the years 1953 and 1954 certain investigations were being made on patients (mental defectives) of the Royal Earlswood Hospital Group with the encouragement of the physician superintendent, Dr. H. R. Ferguson. Part of these investigations involved pneumo-encephalograms, which were carried out in the radiological department of the Redhill County Hospital under the supervision of the director, Dr. H. E. Offord. Altogether 30 high-grade mental defectives voluntarily submitted to the operation. Premedication with phenobarbitone, 1 gr. (65 mg.) an hour before the operation, was given and lunch was replaced by a snack, leaving an interval of three hours for the stomach to settle down. Vomiting, however, proved a serious problem in the early cases, and one patient was severely affected in this way for a week and others were markedly disturbed. Clearly some more specific medication was necessary if the work was to be continued, and dimenhydrinate was chosen on account of its known success in suppressing vomiting due to various other causes.

Two ½-gr. (50-mg.) tablets were given half an hour before the introduction of air into the spinal theca. Happily for the patient, but less happily for the investigator, vomiting was controlled, but no air passed into the ventricles of the brain. This method was repeated several times, and it was concluded that the drug was exerting some action on the foramina in the roof of the fourth ventricle and thus preventing the air from passing through.

In all cases, whether with or without dimenhydrinate, a standardized procedure was carried out by the same medical and technical staff, so that failure was not due to inefficiency. Obviously, a variation of this particular medication was urgently needed, and so the dimenhydrinate was not given until immediately after lumbar puncture and the introduction of the air. As a result air once again successfully passed into the ventricles and the patients were still protected from vomiting. The marked sedative and soporific

effect of this drug was also gratifying, as the patients dozed off to sleep while the films were being taken, remained drowsy for some hours, and seemed oblivious of their recent experience.

These findings may be of interest and value to other workers in this field who may be concerned about the comfort of the patient.—I am, etc.,

Birmingham, 22. G. S. MANSELL.

Intra-arterial Thiopentone

SIR,—Dr. Peter Stuart (*Journal*, November 26, p. 1308) has done great service by once again drawing attention to the tragic results which may occur following the intra-arterial injection of thiopentone.

It is interesting to note that, in nearly every reported case in which there has been permanent damage, there have been two common factors: (1) the thiopentone has been a 5% solution, and (2) the vessel injected has been in the antecubital fossa.

A similar case to that reported by Dr. Stuart which occurred in my practice prompts me to make a plea for a wider use of 2½% solutions and to avoid, whenever possible, the injection of veins in the region of the antecubital fossa. I am sure that, if these two points were rigorously followed, there would be a disappearance of one of the most tragic accidents of anaesthesia.—I am, etc.,

Liverpool, 3. JAMES R. CROSS.

Chlorpromazine Poisoning

SIR,—I write to report a case of poisoning with chlorpromazine in a child of 21 months.

The patient was brought into casualty with a history that she might have taken twenty-five 25-mg. tablets of chlorpromazine. She was comatose, responding only to painful stimuli. There was marked muscular hypotonia with absence of tendon reflexes. The pulse was not palpable. It was decided to wash out the stomach in spite of the child's poor general condition; as large an oesophageal tube as possible was passed. The passage of the tube did not stimulate retching, and at no time during the procedure did the child attempt to vomit. Fifteen pints (8.5 l.) of water were used—of these, the last three gave a clear return. The first 12 pints (6.8 l.) produced a considerable amount of pinkish-white particulate matter with the appearance of almost completely disintegrated tablets. No blood and little mucus or food particles were seen. These washings subsequently gave the same chemical reaction as tablets remaining from the same batch of 50, and chlorpromazine tablets from the dispensary—without any concentration being necessary. The child was taken to the ward. The temperature was normal, the blood pressure was 40 systolic with an unrecordable diastolic.

A cut down intravenous drip on the right ankle was started, using 4.3% glucose in 0.18% saline, containing 4 ml. of noradrenaline to one litre. After initial difficulty due to the child's collapsed state, the drip flow was regulated by the blood pressure, which, two hours after starting the drip, had become 90/40. By this time the child had considerably improved and was semi-rousable, so the drip rate was cut to a minimum (10 drips per minute). Penicillin by intramuscular route was given as a prophylactic measure against chest infection. After 12 hours the child could be persuaded to take drinks of glucose and water. By this time it had been realized that liver damage from overdosage of chlorpromazine had been recorded,[1 2] and so glucose drinks were given, and the child started on daily injections of 2 ml. intramuscular vitamin B. After the first 12 hours of improvement the child became comatose and hypotonic again, the blood pressure falling from a maximum of 110/50 to 90/70. The rate of drip flow was increased, with improvement within seven hours. Two further less severe relapses occurred before complete recovery. During the second period of 12 hours, twitchings were observed, involving the hands, feet, and face. After 48 hours gradual improvement occurred and the child was discharged one week after admission with advice to take vitamin B complex tablets.

Investigations for liver and kidney damage were negative both before discharge and when seen six weeks later. These included liver function tests and microscopy of the urine. No neurological sequelae are yet apparent. Hypothermia was not observed, hypotonia and hypotension being the salient features of the case. It would appear that gastric motility is quickly inhibited following absorption of chlorpromazine, and gastric lavage is specifically indicated.—I am, etc.,

Lincoln. J. A. BEAL.

REFERENCES

1 Grytting, G., *Nord. Med.*, 1954, **52**, 1699.
2 Zatuchni, J., and Miller, G., *New Engl. J. Med.*, 1954, **251**, 1003.

Toxic Effects of Isoniazid

SIR,—With reference to the article by Drs. J. K. Hewat, P. W. W. Leach, and R. W. Simpson on chlorpromazine, reserpine, and isoniazid treatment in mental disorder (*Journal*, November 5, p. 1119), concerning the toxic effects of isoniazid they said that ataxia and convulsions have not been registered in man.

M. Mancini[1] reported two fatal cases due to overdosage, the first by mistake (the patient had 5.5 g. isoniazid) and the second to commit suicide. Both presented convulsions before they died. I myself[2] had a case, a tuberculous man of 68, who presented convulsions during isoniazid treatment. The isoniazid was discontinued. Four months later he again had convulsions when isoniazid therapy was once more prescribed. In his history there was some petit mal, but never convulsions. This is why he presented convulsions even with small doses of isoniazid (300 mg. daily). The convulsions are probably due either to the high concentration of isoniazid in the cephalo-rachidian fluid, or to the activity of his products during the isoniazid's disintegration in the organism.—I am, etc.,

Douglas, I.O.M. G. CHASAPAKIS.

REFERENCES

1 Mancini, M. A., *Minerva med. (Torino)*, 1954, **45**, 529.
2 Chasapakis, G., *Iatr. Athen.*, 1954, **57**, 286.

Delayed Onset of Signs in Extradural Haemorrhage

SIR,—I was interested to read the case report by Mr. P. R. R. Clarke and Dr. D. C. Jenkins on "Delayed Onset of Signs in Extradural Haemorrhage" (*Journal*, November 12, p. 1190).

There can be no question that extradural bleeding can be a very slow process in some instances, and recently in Swansea I have had under my care in the neurosurgical unit two examples of extradural haemorrhage in which cerebral compression was not evident until three weeks and three months, respectively, after a minor injury to the head. In both these cases the collection of blood had become encapsulated and each was, in fact, a blood cyst of large dimensions in the extradural plane.

Such cases illustrate the value of repeated ophthalmoscopy following injury to the head, as the condition develops insidiously and headache may not be a prominent feature until the later stages.—I am, etc.,

Swansea. NORMAN WHALLEY.

Porphyria

SIR,—Earlier this year Drs. G. Dean and H. D. Barnes discussed the subject of porphyria (*Journal*, July 9, p. 89), and if this disorder is anything like as common in Britain as it appears to be in South Africa there may well be several hundred affected people in this country. It is now clear that if these people are given certain drugs, especially barbiturates, or are anaesthetized by thiopentone they are running very serious risks.

As the condition is hereditary it should be possible to locate most potential sufferers. Perhaps porphyria could be made notifiable and other patients previously described before the risks were appreciated could be followed up, where this has not already been done. As early symptoms suggest neurosis, use of the ultra-violet light test for urinary porphyrins—mentioned in a recent article by Drs. A. C. Markus and A. G. Spencer (*Journal*, October 8, p. 883) on lead-poisoning—might be rewarding in psychiatric out-patient departments.—I am, etc.,

Sutton, Surrey. E. SAPHIER.

Sore Throat

SIR,—During the past three years I have noted a series of cases where patients have presented with a "sore throat and fever" without any obvious disease in the visible part of the fauces or pharynx. The patient often complains of headache and the muscular pains associated with an attack of influenza. There is no loss of voice or hoarseness. Further questioning always elicits pain on swallowing as the real cause of the soreness. The exact location of the affected part may be palpated by placing the forefinger on the great horn of the hyoid bone on the side of the throat indicated by the patient.

This condition is found in patients of all ages. It is probably a toxic fibromyositis involving the attachment to the hyoid bone of the hyoglossus and constrictor pharyngis medius muscles. Treatment is symptomatic by warmth to the skin and codeine tablets before meals. The condition usually subsides in a few days. In persistent cases, or where the threshold for pain is low, an injection of procaine solution gives instant relief.—I am, etc.,

Hornchurch, Essex. I. H. J. BOURNE.

Nicotine Dosage

SIR,—I was shocked to read that Dr. John D. Spillane (*Journal*, December 3, p. 1345) had injected intravenously into four sick volunteers 2 and even 3 mg. of nicotine acid tartrate. He does not mention having himself tried such a dose. I was not surprised to learn that after 2 mg. had been injected Case 4 "became pale, perspired, breathed heavily, and was frightened." His symptoms strongly suggest acute nicotine intoxication, which I have myself experienced. Although symptoms were less alarming in his other cases, the degree of tolerance to nicotine induced by previous smoking,[1] and how recently smoking had taken place before the injection, would influence their severity. I found that 0.1 mg. of nicotine sulphate intravenously induced in me quite a powerful nicotine action, yet Spillane used 20 and even 30 times this dosage.

May I suggest that before investigators administer toxic drugs to their luckless patients they first try them on themselves?—I am, etc.,

Wallasey, Cheshire. LENNOX JOHNSTON.

REFERENCE

1 Johnston, L. M., *Lancet*, 1942, 2, 742.

Antenatal Pulmonary Embolism

SIR,—In two recent papers attention has been drawn to the surprising rarity of antenatal thrombophlebitis and to the even greater rarity of antenatal pulmonary embolism.[1 2] The following case therefore seems worth mentioning.

A woman, aged 36, with a history of two previous normal pregnancies, was seen by me in July, 1952. She was then eighteen weeks advanced in her third pregnancy. All findings were normal, and progress was uneventful until the 27th week, when she developed a superficial thrombophlebitis on the dorsum of the left foot. She was advised to rest and apply local heat to the part. One week later there were signs of subcutaneous thrombophlebitis on the inner side of the calf. She was ordered to bed forthwith, and treatment with kaolin poultices and daily intramuscular penicillin was given. Despite this, the condition began to spread upwards along the saphenous vein to the thigh. There was no oedema, nor any other evidence of deep venous thrombosis. The use of anticoagulants was thought to be contraindicated, but a consultant surgeon was asked to see her with view to ligation of the vein. By this time, however, the condition appeared to be subsiding, without further extension, and ligation was not advised. The patient was kept at complete rest and the treatment continued as before. A week later, while still in bed, she suddenly collapsed and died immediately. There was no doubt that she had succumbed to a massive pulmonary embolus.

The incidence of antenatal thrombophlebitis, in midwifery practice as a whole, must surely be greater than hospital records alone would suggest. Yet death from pulmonary embolism during pregnancy would seem to be excessively rare, both in domiciliary and hospital obstetrics. It is quite evident that the number of these cases in which anticoagulants have been given is, as yet, too small to provide the basis for a reliable opinion as to their value. From a general practitioner's standpoint, however, it is obvious that admission of the patient to hospital is strongly advisable. In a case where the process is spreading, but still confined to a superficial and easily accessible vein, as in the one here described, there could hardly be much risk in ligating the vessel, and a fatal outcome might be avoided, without the additional hazard to the foetus which anticoagulants have been found to introduce in some cases.—I am, etc.,

Newtownards, Co. Down. C. G. WARNOCK.

REFERENCES

1 Gordon, R. R., and Dean, T., *British Medical Journal*, 1955, 2, 719.
2 Sibthorpe, E. M., ibid., 1955, 2, 1063.

Ban on Heroin

SIR,—The marked division of opinion among doctors as to the indispensability of heroin is at first sight difficult to understand, but the explanation I think lies largely in the fact that very few of us are really in a position to know, from our own limited experience, the true facts of the case. And this applies as much to consultants and specialists as to general practitioners. One cannot help thinking that very few of those in favour of the ban, including the members of the Medical Advisory Committee of the Ministry of Health, can have had much experience of the type of case for which heroin is chiefly required—the last incurable stages of cancer. Cancer is a vast subject, and even a surgeon who specializes in that disease is naturally mainly concerned with its earlier stages, and may have little time or opportunity to study the details of the management and care of patients towards the end. I would go further and say that, apart from the patients themselves, the people best qualified to know the truth in this matter are not doctors at all, but nurses—the matrons and ward-sisters of the special institutions where cancer patients go to die. A doctor who merely visits a hospital, however frequently, cannot have the same intimate understanding of the individual patient's reactions to different drugs as the nurses who carry out the treatment and are with the patients day and night.

Up to the time of my retirement from general practice a year ago I was for 13 years in charge of a small 32-bed hospital, St. Columba's, in London, entirely devoted to the care and treatment of hopeless cancer cases, and I visited them every day. Rather more than 200 new patients passed through our hands each year, so that my experience of these cases was an exceptionally large one. Cancer unfortunately takes a long time to kill, and the last hopeless stages may continue for many months. Of course we were familiar with all the pain-relieving drugs. For some of our patients the less potent ones were sufficient, at any rate for a time; but most of them sooner or later required either morphine or heroin to make life at all bearable. Many were seriously upset by morphine and could only be kept comfortable by heroin. By trial and error and individual study of each patient (to a degree probably only possible in a small institution) we found out how best to bring relief. The dosage required was often a large one, and might have to be repeated several times a day for months at a time.

Well cared for both physically and spiritually, with a great deal of kindness and plenty of drugs, these dying patients remained on the whole surprisingly comfortable and happy. But, inadequately treated, cancer in its later stages can be quite as horrible as it is commonly supposed to be. It would be a cruel shame if thousands of innocent but unfortunate people in this country were submitted to severe, prolonged, and unnecessary pain and suffering for the supposed benefit of drug addicts in other lands. I may add that in my ordinary private practice I hardly ever had occasion to use this drug.—I am, etc.,

Jersey. NORMAN A. SPROTT.

SIR,—The emotions let loose through the banning of heroin go strange ways, as Dr. J. H. Beale's letter (*Journal*, December 10, p. 1450) shows. May I point out to him that the United Nations Organization is not a sinister organ-

ization bent on "world government by any means in their power," but an organization formed by the governmental representatives of the various member States, alas not yet universal, whose only power of coercion so far is, regrettably, only moral, and whose aim among other things is to prevent war and increase the health and happiness of mankind?

Belonging to such an international organization, as Great Britain does, means voluntarily giving up part of the country's sovereignty and thus forming new bonds of international loyalty, previously unthinkable. If Dr. Beale regrets this development he is still thinking in pre-first-world-war terms.—I am, etc.,

Nottingham. G. FIELDING.

SIR,—On September 18, in a letter to the *Scotsman*, I protested against the proposed ban on heroin. I pointed out that the drug was used by most doctors only rarely and mainly in distressing or painful terminal illness, when it can sometimes give great mental tranquillity as well as pain relief.

I also remarked that Dr. H. Berger (who is a consultant in internal medicine to the U.S. Public Health Service) had given an address at the Third International Congress on Criminology in this country in September. I am surprised that more publicity was not given to his remarks at that time and since. In that address he said, or was reported as saying, that he was sorry to see us making the same mistake as his own country, which banned heroin thirty years ago and to-day has an enormous illicit heroin addiction problem compared with anything here. He thought the ban would merely open the field to the illicit peddling of heroin here.

Fortunately there are now some faint signs that the Government may be prepared to reconsider this matter. Let us indeed hope so, for the ban can only increase heroin addiction through illegal channels, and that at the cost of denying the drug to those few sufferers who might benefit from its medical use. One thinks particularly of the more distressing cases of terminal illness who must end their days at home in mental if not physical misery because of the lamentable shortage of hospital beds for this type of illness.—I am, etc.,

Edinburgh, 1. ROBERT C. MCLAREN.

Physiotherapy

SIR,—It is wise, before a discussion on how to administer a remedy, to ascertain first if it is any use at all. Mr. R. H. Beckett is, I am sure, right when he avers that different ways of giving radiant heat have slightly different physical effects (*Journal*, December 10, p. 1449). But surely the point is whether radiant heat has any medical value at all, however given. If (as I maintain) it is a pure placebo, the way it is given is immaterial; the only criterion is whatever pleases the patient most.

The common indication for physiotherapy is maintenance or restoration of power and painless mobility in the moving parts. Heating the skin when the lesion lies more deeply within the moving part involves treating the wrong structure. Medicine aims at a diagnosis leading, whenever possible, to such treatment as affects the lesion. Hence radiant heat may possibly be useful in skin conditions, but cannot be indicated in the treatment of the moving parts, for the simple reason that they lie out of reach, whether the rays are administered with much circumstance by a physiotherapist or in a rough and ready way by the patient to himself at home.

Radiant heat has a positive disadvantage, as well as the negative one of treating the wrong tissue. Its use means that rational treatment is being denied the patient, though he may not realize it. Much of physiotherapists' work is stultified in advance by a prescription of heat-and-massage or heat-and-exercises, when accurate measures that do reach the lesion are indicated. After all, it was only before the days of surgery that appendicitis was treated by a hot poultice. Nowadays, by means of precise exercises, deep massage applied to the lesion itself, manipulation, traction, local analgesia, or hydrocortisone, an effective treatment can be brought to bear on almost any disorder of the moving parts. Surely this renders radiant heat a complete anachronism.—I am, etc.,

London, W.1. JAMES CYRIAX.

Treatment of Post-herpetic Neuralgia

SIR,—As a teacher and examiner of the Chartered Society of Physiotherapy for about 15 years, I feel that the technique of treatment used for histamine iontophoresis, as suggested by Dr. L. Engel (*Journal*, December 3, p. 1391), is, to put it mildly, most extraordinary.

Surely the improvisation of "saucepan cleaners—enclosed in a wet lint-bag" for electrodes is both unnecessary and potentially dangerous. Is it of no account that every trained physiotherapist, in order to prevent dangerous local and general effects (of which perhaps Dr. Engel is not aware), uses a special size of pad electrode and a maximum current of 100 milliampere minutes (10 mA. for 10 min.)? This maximum is, of course, progressed to very carefully by about a minute a treatment. I might also add that the English used in the letter would leave the beginner in doubt as to where the urticarial rash has to appear.

Is it also really possible that Dr. Engel does not know that histamine ionization has been used as a pain reliever in post-herpetic neuralgia and other conditions for at least 20 years? And this carried out with considerable success in spite of the absence of culinary equipment.—I am, etc.,

London, W.1. JOYCE MASSEY.

Post-partum Haemorrhage

SIR,—Dr. J. G. Dumoulin's letter (*Journal*, December 10, p. 1449) refers to the reduction in the post-partum haemorrhage rate which can be obtained by the use of intravenous ergometrine given at the time of the crowning of the foetal head. As he states, similarly good results can be obtained by the use of intramuscular ergometrine with hyalase.

At Hackney Hospital we have been giving ergometrine, 0.5 mg. intramuscularly, with the crowning of the head, routinely at all deliveries except those where intravenous ergometrine seemed specifically indicated by reason of long labour, general anaesthesia, forceps delivery, multiple pregnancy, maternal anaemia, ante-partum haemorrhage, grand multiparity, etc. In 836 consecutive vaginal deliveries recently examined there were 30 post-partum haemorrhages—an incidence of 3.5%. In 8 of these cases (27% of the total incidence) the ergometrine had been omitted because of precipitate delivery or other reasons; 60% of the haemorrhages (18 cases) were less than 30 oz. (0.9 l.) in amount, and 66% of them (20 cases) followed normal labours. I believe that our figure of 3.5% can be reduced to about 2% by closer adherence to the method outlined.

The wholesale price of one ampoule of ergometrine is about 6d., while the ergometrine and hyalase preparation costs about 3s. 4d. per injection. I suggest, Sir, that the reduction of post-partum haemorrhage can thus be achieved by the above method more easily than by the intravenous use of ergometrine, and at considerably less expense than the routine use of ergometrine and hyalase would entail.—I am, etc.,

London, N.W.3. H. E. REISS.

"Modern Health Series"

SIR,—As my father is not here to reply to your reviewer's remarks about this series (*Journal*, December 17, p. 1489), I feel I should try to do so, even though I have a vested interest as being chairman of the firm which publishes the books.

The questions your reviewer raises are natural ones, but they can never be precisely answered either way. Those interested would, however, have been better able to make up their minds on the subject had your reviewer quoted—instead

of half a sentence—the whole of my father's introductory note which appears in every volume of the series and every prospectus. This runs as follows, and correctly epitomizes the spirit in which the books are written :

"It is natural and reasonable for a patient to be interested in the disease from which he suffers. Under modern conditions this natural curiosity is too often satisfied in a catchpenny manner, incomplete and misleading where it is not actively harmful; so that doctors often find themselves having to waste precious time in disabusing patients of false beliefs about their ailments.

"It is the object of this series of books to give precise, authoritative information; to take the patient into the doctor's confidence so that both work together to get the patient better; to explain things simply and intelligibly; to offer sufferers whatever hope the most up-to-date medical knowledge can honestly offer; in short to tell the truth about diseases as it has never been told to the general public in print before.

"The series is designed to give general background information only. The books are not courses of self-treatment; nor will the writers reply to any queries addressed to them by the general public. Consult your own doctor about your own case."

I am not fitted to comment on questions of professional etiquette, but can say that when the idea of publishing this series was originally referred to the General Medical Council in 1953 no objection was raised. I should like also to make clear that it was my father's wish to cover in this series only those ailments and conditions of a semi-chronic nature with which a sufferer may have to live over a period of months or years, and about which he may reasonably—after a hundred years of popular education—require some reliable basic information. It remains our intention to limit the series in this way.—I am, etc.,

London, W.C.2. HORDER.

Homosexuality and Prostitution

SIR,—I have read the B.M.A.'s memorandum on homosexuality and prostitution (*Supplement*, December 17, p. 165) and it has caused me a great deal of apprehension. As I remember it, the Hippocratic Oath charges us with alleviating suffering and at all times loyalty to our patients—which finds its expression in "professional secrecy" as the supreme test. Our oath says nothing about legislation, administration, or morals—they are, in our tradition, not our business except that part of conduct which concerns our own. This B.M.A. report seems to vacillate between this genuine desire to help and between legislation; the latter is surely for the people in general to determine: if its morals or ethics are "lax" it is not for the men of medicine to say so; it is for the people to determine what should be their *mores*. If we do not know what makes a homosexual and what cures him, we should say so, and we then should leave it to others to protect society from his corruption as necessary. It may be worth remembering, in this context, the problem of Galileo: whether the sun revolved round the earth or vice versa was a question of faith, and therefore ethics, until his day—he was accused of heresy when he proved that the earth revolved round the sun.—I am, etc.,

London, W.14. S. L. SHERWOOD.

Chronic Perionychia

SIR,—Dr. F. F. Hellier (*Journal*, December 3, p. 1358), in quoting the surgical textbook of Handfield-Jones and Porritt,[1] does not sufficiently stress the distinction between acute staphylococcal paronychia, in which infection is deep to the nail-root, and "chronic perionychia," in which infection is between the nail-fold and the nail-root. It is to the former condition that the surgeons refer and incision may be necessary, but surgery is not indicated in the latter.

Like Dr. C. Howard Whittle (*Journal*, December 17, p. 1499), we have always found monilia in a series of cases of chronic perionychia examined microscopically, and when these have been cultured at the mycological department, St. John's Hospital for Diseases of the Skin, *Candida albicans* has grown.

In our cases, as in those of Dr. Hellier, a history of "dead fingers," cold hands, and chilblains has been common. However, in 13 of our patients in whom Dr. J. Bishop did the reactive hyperaemia test there was no difference, as compared with an equal number of patients not so affected, in the time taken for the flush to appear round the nail. In the patients examined, then, chronic perionychia would not appear to herald an organic vasoconstriction (communicated as part of a paper read to the Canadian Dermatological Association, Niagara Falls, 1955).

If the condition is a monilial infection the dyes should be helpful in treatment. A paint containing brilliant green is recommended by Dr. Hellier, but, as this form of "green fingers" is unlikely to be popular, colourless preparations are preferable. We have had good results with "monphytol," which contains boric acid, salicylic acid, undecylenic acid, and methyl salicylate in a volatile base. One or two drops of the solution are placed well down into the pocket between the nail-fold and root with the finely flattened blade of an orange-stick twice daily. Pain may go within a few days. The treatment should be supplemented by the other measures outlined by Dr. Hellier and your correspondents. —We are, etc.,

G. B. MITCHELL-HEGGS.
London, W.2. M. FEIWEL.

REFERENCE

[1] Handfield-Jones, R. M., and Porritt, A. E., *Essentials of Modern Surgery*, 1948, 3rd ed., p. 252.

Flavoured and Sweetened

SIR,—I wish to bring to the notice of medical practitioners and manufacturers the possible danger in disguising drugs. I recently had to attend a child of 2 who had recently taken 30 gr. (2 g.) of "flavoured and sweetened" junior aspirin, which at initiation the mother had described as "sweets." The stomach was washed out and the child recovered, but bore resentment against the necessary use of a gag at this early but tooth-bearing age.—I am, etc.,

London, W.5. GEORGE H. ALABASTER.

Restoration of Breathing after Presumable Death

SIR,—The following case may be of interest. A male patient of mine, aged about 68, with a history of chronic bronchitis and asthma and phlebo-thrombosis of the right calf veins, telephoned me from his flat at about 1 p.m. requesting a visit. He did not request an immediate nor an early visit, neither was there anything in the tone of his conversation to suggest urgency. I arrived at 3.20 p.m., during my round of visits. The lock to the door of his flat was left unfastened. On entering I found the room saturated with coal-gas escaping from a gas poker, the patient sitting in a chair, his head having fallen back over the back of the chair, his eyes wide open, lifeless; there was no breathing and the pulse could not be felt. The patient was presumably dead, but, having dealt with the escaping gas, I gave an intramuscular injection of 2 ml. of nikethamide and a hypodermic injection of adrenaline hydrochloride 1 in 1,000, 8 min. (0.5 ml.), and applied artificial respiration. After about 20 minutes, to my surprise the patient gave a slight gasp and breathing recommenced. I had him removed to hospital. A few days after admission he became fully conscious, but later relapsed into a state of confusion. He had developed gangrene of the right foot, also he had a blood urea of 300 mg. per ml. He died ten days after admission.

Post-mortem examination revealed bronchial pneumonia, pulmonary infarction, phlebo-thrombosis of right femoral vein, with thrombosis of the femoral artery due to arteriosclerosis, and gangrene of the right leg. It was not regarded as a case of suicide. The interesting point is, I think, that, if there is any possibility that a patient may have only just ceased to breathe and have a pulse or heart beat, though apparently absent, it is well worth while doing everything possible to restore life.—I am, etc.,

London, N.W.1 M. D. RIPKA.

Obituary

CYRIL FERNANDO, C.M.G., O.B.E., M.D., M.R.C.P.

Dr. Cyril Fernando, who died in hospital at Colombo on November 26 at the age of 55, was one of Ceylon's leading physicians.

Born at Colombo on April 30, 1900, Cyril Francis Fernando left St. Benedict's College in that city to receive his medical education at University College Hospital, London, where he came under the influence of Sir Thomas Lewis, Sir John Rose Bradford, and Dr. H. Batty Shaw. He graduated M.B., B.S. in 1925 and took the M.R.C.P. in the following year. On his return to Ceylon soon afterwards he joined the Colonial Medical Service and for a short time was employed at a provincial hospital in the south of the island before becoming medical registrar at Colombo General Hospital. He returned to his old medical school in London in 1929 and gave evidence of his unusual ability by winning the gold medal when he proceeded to the degree of M.D. Later in 1929 he was appointed physician to out-patients at Colombo General Hospital and rose steadily on the visiting staff of the hospital until he became a senior member. He was also a teacher and examiner in medicine in the Ceylon Medical College and, later, in the University of Ceylon.

Fernando's activities were not restricted to hospital duties and consulting practice. He took an active interest in the Ceylon Medical Association (then the Ceylon Branch of the British Medical Association), having been honorary secretary and treasurer of the Branch from 1930 to 1932, a member of the council in 1933, 1934, and 1949, vice-president in 1942, and president in 1948–9. He was one of the delegates from Ceylon to the first British Commonwealth Medical Conference, held in London in 1948. In spite of ill-health he accepted the appointment of chairman of the Ceylon Hospital Sweeps Board, to the work of which he brought mature experience and wisdom. His services to medicine were recognized by his appointment as O.B.E. in 1949 and as C.M.G. last January.

We are indebted to Professor G. H. COORAY for the following appreciation:

As a teacher Cyril Fernando was loved and respected by his students, who will miss his pronouncements, expressed with such clarity and precision. His sayings were often tinged with wit and became aphorisms among students of the medical faculty. To the bedside he brought the benefit of a wide experience of disease and understanding of human nature. To his patients, who were drawn from the poorest as well as the richest of the land, he was equally kind and sympathetic. Cyril, as he was known to his friends and colleagues, inspired such confidence that rarely was a diagnostic complexity, either in the hospital wards or in private nursing-homes, cleared up without his co-operation. Although he reached the top of the profession, he never forgot his modest beginnings, and very recently he donated a science laboratory to the school where he received his elementary education.

Though not in the best of health in recent years, he showed no sign of it in his active and energetic life. He was warned to go slow after an operation in London in 1952, but he was not the type of man to let his patients down. Early this year he was again in London for treatment, and his colleagues advised him to retire from hospital work. He probably realized that this was correct advice, but again he demurred, for he dreaded a life of inactivity. Instead, he took a few weeks' leave and entered the General Hospital as a patient, and he ended his days in the institution that had been part of his life for over a quarter of a century. His sense of humour never deserted him. Faced with any trial or tribulation, he rarely failed to find a way out with a smile. In humour he found courage and strength to face the end that he knew was inevitable in his last days. Only a few minutes before he died, when he realized that his breathing was failing, he made a last quip—at the expense of the oxygen apparatus beside him. Undoubtedly Ceylon has lost one of her greatest physicians, and a host of friends, colleagues, and patients salute his passing.

C. H. ALLEN, O.B.E., M.B., F.R.C.S.Ed.

The death occurred on December 10 of Mr. C. H. Allen in the General Hospital, Nottingham, to which he had given many years of service as honorary surgeon. He was 78 years of age.

A farmer's son from Metheringham, Lincolnshire, Charles Henry Allen was a medical student at Edinburgh University, where he graduated M.B., Ch.B. in 1900. In the same year he joined the staff of the Nottingham General Hospital as assistant house-surgeon, and, having obtained the Fellowship of the Royal College of Surgeons of Edinburgh in 1906, was appointed to the honorary staff of the hospital in 1907. In his early days Mr. Allen was an active Territorial officer, and at the outbreak of the first world war in 1914 was a captain in the 3rd North Midland Mounted Brigade Field Ambulance. He went to Egypt with the brigade in the spring of 1915, but later was detached from the field ambulance to command the Ras-el-Tin military hospital in Cyrenaica. He was three times mentioned in dispatches for his services in the field, twice by Lord Allenby, and was appointed O.B.E. and awarded the Order of the Nile (Fourth Class).

After the war he returned to his work at Nottingham as honorary surgeon at the General Hospital. Later he became senior surgeon and chairman of the medical committee of the hospital. He was also for many years consultant surgeon to the City Hospital. He was a Fellow of the Association of Surgeons of Great Britain and Ireland, and in 1931–2 president of the Nottingham Medico-Chirurgical Society. Because of the second world war, and at the request of the hospital board, he continued his work as a surgeon for four years past the retiring age, and he eventually gave up active consultant work in 1946. A member of the British Medical Association for forty-two years, he served as a vice-president of the Section of Surgery when the Association held its Annual Meeting at Nottingham in 1926. He was also chairman of the Nottingham Division in 1927–8 and president of the Midland Branch in 1933–4.

Mr. JOHN F. SHEEHAN writes: "C.H.," as Allen was known to all of us at "the General," had a shrewd clinical sense and was essentially a safe surgeon. Conscientious to a high degree, he did not stint himself in the care he gave to his patients: the more ill the patient, the harder he fought for him. He had an informed mind on many subjects, and since he had a lively sense of humour he could be a most entertaining companion. He spoke little of his own attainments. He was keenly interested in sport, his chief recreation being hunting, and he especially loved a good horse. For many years he was a prominent member and follower of the Blankney Hunt in Lincolnshire. He was also an enthusiastic, though indifferent, golfer, but was widely read on the game, as he was on all subjects in which he took an interest, and this applied in even greater measure to his chosen profession. He was a staunch friend and will be remembered with affection by his own colleagues and his wide circle of friends.

Dr. D. J. BROWNE, who died in St. John's Hospital, Wandsworth, on October 24 after a distressing illness, was a native of Moneymore, Co. Derry. With a brilliant school record behind him, David John Browne entered the old Royal

University of Ireland in 1897 and graduated in arts three years later. Proceeding to the Assembly's College, Belfast, he studied classics and divinity, winning many prizes and medals. In 1903 he went to Edinburgh University, and a year later entered the ministry of the Established Church of Scotland. Fulfilling a lifelong ambition in 1915, he entered Trinity College, Dublin, as a medical student and graduated M.B., B.Ch. in 1921. Subsequently he was appointed house-surgeon at Londonderry Infirmary, and afterwards settled at Rotherhithe, in south-east London, where he remained in general practice until 1951, when he was obliged to retire owing to ill-health. He was devoted to his patients and his practice and seemed to enjoy every moment of his medical career. His wide cultural background, ranging from philosophy to modern languages, made him a stimulating companion. His gentleness, sincerity, and integrity endeared him to his medical colleagues, to whom his loyalty never wavered. At divisional meetings of the British Medical Association—he was chairman of the Camberwell Division in 1938–9—his presence is sadly missed by his general-practitioner friends, for he not only took a scholarly interest in medical progress but had a far-seeing concern for the future of the profession.—W. B. P.

The sudden death from coronary thrombosis at Twickenham on November 30 of Dr. SAMUEL HALL, three weeks after his retirement from general practice at Huddersfield, came as a great shock to his many friends in Yorkshire. He was 59 years of age. Born in Ulster on February 20, 1896, Samuel Hall studied medicine at the Queen's University, Belfast, and graduated M.B., B.Ch. in 1919. He came to England in the following year and served as house-surgeon first to Mr. B. Holroyd Slater and then to the late Mr. Basil Hughes at St. Luke's Hospital, Bradford. He settled in general practice at Golcar, Huddersfield, in 1924, and soon proved himself to be a very sound clinician. His conscientiousness and his devotion to the welfare of his patients, allied to a happy and cheerful disposition, made him a first-rate family doctor. A member of the British Medical Association for thirty-five years, he was chairman of the Huddersfield Division in 1949–50. He was a keen follower of Rugby Union football, taking great interest and pride in the distinguished career of his son, Mr. N. M. Hall, a former England captain. The affection and respect in which he was held by his medical colleagues and patients was very evident on his retirement and at the funeral and memorial services. He was very fortunate and happy in his home life, and our deep sympathy is extended to his widow and two sons.—W. E. D. C.

Mr. HAROLD GEORGE DOWNER, who died suddenly in Hove General Hospital on December 7 at the age of 62, was born in Melbourne, Australia. He was a medical student at Melbourne University, graduating M.B., Ch.B. in 1917. During the later stages of the first world war he served with the Australian Forces in France, coming to Britain, as did many of his compatriots, at the end of the war to further his professional experience. After some three years spent as a much-esteemed resident at the Royal Sussex County Hospital and subsequently at Hove General Hospital, he settled in Hove in general practice with the ultimate intention of taking up otolaryngology. Having obtained the D.L.O. in 1927, he thereafter confined himself to his chosen specialty. In 1928 he was appointed assistant surgeon to the Sussex Throat and Ear Hospital and surgeon to the ear, nose, and throat departments of Hove General Hospital and Worthing Hospital. Five years later he was elected to the staff of the Royal Sussex County Hospital, to which he was always particularly attached. In the due course of time he became senior otolaryngologist to both Brighton and Lewes and Worthing hospital groups. He was a man of restless activity, and numerous other institutions benefited from his services, notably the Sussex Eye Hospital, the Brighton School for the Partially Deaf, and also, during the last war, the hospitals of Crawley and Ryde. He had been president of the Brighton and Sussex Medico-Chirurgical Society and was to have been a vice-president of the Section of Otorhinolaryngology at the Annual Meeting of the B.M.A. in Brighton next year. Harold Downer was justly proud of being an "Aussie," loved cricket, golf, and bridge, was a great reader, and had a formidable knowledge of the literature of otolaryngology. His juniors might at times have been intimidated by his gruff manner, but he would take infinite pains to help them in every way. His numerous friends were filled with admiration at the amazing fortitude with which he battled with ill-health for many years, coming back more than once from the brink of eternity to carry on grimly with his work. Our deepest sympathy goes to his wife, whose devoted care had so long sustained him, and to his son and daughter.—T. S. A.

Dr. DAVID GREVILLE WILLIAMS died at his home at Taffs Well, Glamorganshire, on December 14, two days after his 66th birthday. A native of Carmarthenshire, he was educated at Carmarthen Grammar School and King's College, London, where he graduated B.A. in 1913. During the first world war he served with the Royal Engineers and in the Royal Flying Corps. For two or three years after the first world war he was a master at Stroud Grammar School, and he did not begin the study of medicine until 1921, when he became a medical student at the Welsh National School of Medicine. He went on to King's College Hospital to do his clinical work, and qualified in 1925. He then went immediately as an assistant in a colliery practice at Abercynon, and in later years he wrote that a simple course in first aid when a student would have been a great help to him at the beginning of his career as a general practitioner. He had to learn quickly, for his principal took the view that if a man had satisfied the examiners that he was fit to be a duly qualified medical practitioner then that man was obviously fit to look after the patients. After a year in this assistantship Dr. Williams decided to buy a small colliery practice at Nantgarw and Taffs Well, in Glamorganshire. The colliers at that time were tied to the colliery doctor, who was paid by a levy from the workmen called "surgeon's pence." The work was hard and exacting, but extremely interesting and varied, and the practice expanded steadily. In later years Dr. Wifliams held the post of industrial medical officer at the Treforest Trading Estate, and he was a part-time regional medical officer under the Welsh Board of Health. He was keenly interested in first-aid work, and lectured to the members of the St. John Ambulance Brigade in his area. An active member of the B.M.A., he served on the local executive committee for many years, and during the years 1949 to 1950 he was a very popular chairman of the Cardiff Division. He enjoyed a game of golf and was a popular member of the Radyr Golf Club. In 1951 Dr. Williams contributed an article on colliery practice in the educational number of the *British Medical Journal*, and in this he showed how hard work in an industrial area had its compensations, even if not financial ones. Writing about his student days at King's, he remarked how fortunate he had been in his chiefs and tutors. "It is not the brilliant diagnosis, the meticulous care given to an operation . . . that I can recollect most clearly now. It is the insistence of my tutors on a thorough examination of the patient, and their insistence on the same phrase in all departments, 'Examine the patient.'" During the thirty years of his work among the miners Dr. Williams saw many changes, and he was impressed by the recent increases in the amount of care given to the welfare of the workers and the attention given to restoring the injured to health and fitness. In particular he found the provision of an excellent ambulance service a very great boon to a general practitioner in an industrial area.

Dr. MORGAN WILLIAMS writes: Dr. Williams combined high intelligence and charm with kindness and consideration for others. He was a good doctor and a devoted and loyal friend who will be greatly missed by his patients and colleagues. His real pleasures in life were connected with his work and with his home. His son is a final-year medical student at University College Hospital, and his daughter is on the nursing staff at the Middlesex Hospital. To them and to his widow we offer our sincere condolences.

Medical Notes in Parliament

PRIVILEGE COMPLAINTS FAIL

References in the B.M.A. pamphlet *Homosexuality and Prostitution* were raised as a matter of privilege in the House of Commons on December 19. Lieutenant-Colonel M. LIPTON (Brixton, Lab.) complained about the passage:

"Other ways in which male homosexuals arouse the hostility of the public include their alleged tendency to place their loyalty to one another above their loyalty to the institution or government they serve, and, on the part of homosexuals in positions of authority, to give preferential treatment to homosexuals or to require homosexual subjection as expedient for promotion. The existence of practising homosexuals in the Church, Parliament, Civil Service, Forces, Press, radio, stage and other institutions constitutes a special problem."

He said that charging M.P.s with conduct rendering them unworthy to sit in Parliament was a breach of privilege. In view of the present state of the law, whatever their views might be, any assertions of the existence of practising homosexuals in Parliament must be regarded as serious.

The SPEAKER said that he had ascertained that the pamphlet was published on December 14, and extracts appeared in the Press on December 16. According to the rules of the House the matter should have been raised on that day. That did not prevent Lieutenant-Colonel Lipton putting down a motion for consideration by the House.

Lieutenant-Colonel LIPTON also complained of an article in the *People* on December 18, in which, under the headline "Vice in Parliament," it was stated:

"Last night grave new disclosures were made by a famous doctor about vice in Parliament. They follow publication of a report on practising homosexuals at Westminster. The doctors who reported last week on the existence of practising homosexuality in Parliament knew of actual cases of homosexual members when they published their findings. This disclosure was made to the *People* yesterday by a well-known psychiatrist, a member of the special committee of the Council of the B.M.A. which issued the report."

He handed to the Speaker a cutting from the newspaper. The SPEAKER pointed out that it was necessary to produce the whole document. He reserved his decision until the following day, when he stated that it was a clear rule that the whole document must be produced.

The complaint therefore failed on the technical point.

HEROIN

Hospital Stocks

Dr. A. D. D. BROUGHTON (Batley and Morley, Lab.) asked the Minister what was his estimate of the quantity of heroin that had been stocked by hospitals since it became known that the further manufacture of the drug was likely to be banned. Mr. IAIN MACLEOD said he knew that some hospitals had increased their stocks, but he could not without extensive inquiry estimate the increase throughout the country.

Dr. BROUGHTON said that many hospitals, including some of the greatest teaching hospitals, had been increasing their stocks of heroin since the threat to ban manufacture. Was that not strong evidence that many of the most distinguished members of the profession held the opinion that there was no suitable and equally effective substitute? Would the Minister ensure that that was made abundantly plain in the coming White Paper? Mr. MACLEOD replied that it was evidence of a conflict of view in the medical profession which they had always known existed.

Lieutenant-Colonel LIPTON (Brixton, Lab.) asked which London hospitals had, in view of the intended ban, increased their normal stocks of heroin; and whether the Minister had approved the additional expenditure thereby incurred. Mr. MACLEOD said the information was not available to answer the first part of the question. There would of course be no question of approval to additional expenditure for such a purpose, but authority was not required for the purchase of drugs within the total of the approved budget.

Lieutenant-Colonel LIPTON asked if it was not deplorable that a small group of doctors should have made up their minds to sabotage the ban the Government intended to impose. Was the Minister going to make clear that further attempts to evade the ban would be viewed with disfavour by him? Mr. MACLEOD: This is a difficult question. We do not control the stocks of drugs which a hospital chooses to purchase, and even after reflection I do not want to issue any form of instruction on the matter. That would be going too far. On the other hand, it is right to say that this is an expenditure of public money, and that therefore those who spend it should take into account the views of the Government.

Sources of Advice

Dr. BROUGHTON asked the Minister from which body of medical opinion he had sought expert advice since meeting a deputation from the British Medical Association in July, 1955. Mr. MACLEOD replied, "None." No medical considerations were put forward by the Association which had not already been before the Standing Medical Advisory Committee.

Dr. BROUGHTON asked if the Minister did not think that when he had had such strong representations from the B.M.A. opposing the proposal he should have put the matter again before the Medical Advisory Committee, or better still the Royal Colleges, and informed them of the protest of the B.M.A. and asked them to consider the matter. Mr. MACLEOD said that the Chairman of the Council of the B.M.A., who led the deputation protesting against the ban, was one of those present at the meeting who concurred in the advice that the ban should be imposed. The considerations put forward were not strictly medical ones on which it might be necessary to have further advice, but related essentially to professional matters.

Sir ROBERT BOOTHBY (Aberdeenshire, East, Lab.) said the Chairman of the B.M.A. Council had since withdrawn and retracted the views he expressed as a member of the advisory committee. Was it the intention of the Minister not to have further consultations with the B.M.A., the Medical Research Council, or anyone? Mr. MACLEOD: No.

Dr. EDITH SUMMERSKILL (Warrington, Lab.) said that to do as Dr. Broughton had suggested would be quite improper; it would be trying to bring pressure to bear on the Standing Advisory Committee by the B.M.A. The Standing Advisory Committee was representative of the highest medical thought in this country, and to bring pressure of that kind to bear on it would be grossly unfair. Mr. MACLEOD said he was grateful for that. Perhaps he should make it clear that the Government believed they went to the right body to get this advice, and the committee was a body of the greatest distinction. It was on the basis of that advice that he had advised the Home Secretary.

Illicit Traffic

Dr. DONALD JOHNSON (Carlisle, Con.) wanted to know what was the number of registered heroin addicts licensed to receive the drug by Health Service prescription; and what arrangements the Minister proposed to make in respect of these people subsequent to the ban on the drug. Mr. MACLEOD said that heroin addicts were not registered or licensed to receive heroin, and a patient received heroin under the Health Service only if his doctor prescribed it as being necessary for his treatment. If heroin were not available it would be for the doctor to decide which, if any, of the various alternative drugs should be prescribed.

Dr. JOHNSON asked the Minister to be mindful of the danger that these people, many of whom were chronic addicts, would form a hard core for illicit traffic in drugs if heroin were stopped. Mr. MACLEOD said the number of

addicts in this country was known to be so small that he did not think they would provide any appreciable traffic in an illicit trade.

Chronic Bronchitis and Tuberculosis

Mr. SOMERVILLE HASTINGS (Barking, Lab.) asked the Minister of Health on December 19 whether he was aware that the death rate from chronic bronchitis in adult males varied greatly in different localities, and in the same locality in those engaged in different industries; and whether he would cause an inquiry to be made into the cause and prevention of this malady. Mr. IAIN MACLEOD replied that he knew of these facts. Some aspects of the problem were already being considered by the Standing Medical Advisory Committee and, he was informed, by a working party of the Medical Research Council.

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked whether the Minister had noted the lowering of the death rate from tuberculosis in recent years, while the death rate from chronic bronchitis and allied lung disorders was rising; and whether he would give consideration to using the services of the antituberculosis clinics and their skilled medical personnel to deal with these latter disorders. Mr. MACLEOD said that he had noted the encouraging fall in the death rate from tuberculosis, but the numbers of new cases notified had not been falling so quickly and still made heavy demands on the chest clinics. Nor did he accept the suggestion that the death rate from chronic bronchitis was rising.

Dr. STROSS suggested that if they were successful in further combating tuberculosis there was a possibility that the staffs and premises of these clinics might no longer be needed. His point was that as there was much chronic bronchitis and allied chest disorder those staffs should be considered for dealing with these diseases. Mr. MACLEOD said that the figures of bronchitis must be studied with great care, because they were not always comparable, owing to the changes in the international classification. It was true that they could look forward to having a considerable increase in resources from the fact that the beds for tuberculous patients were not so much used as they had been, but he did not think that time had yet come.

Infection in Lodging-houses

Mr. HASTINGS asked the Minister whether his attention had been called to recent evidence indicating that a not inconsiderable proportion of those living in common lodging-houses and reception centres were suffering from pulmonary tuberculosis and apt to infect others; and whether he would call the attention of local authorities to the desirability of *x*-ray examination of such people and provision for the necessary treatment. Mr. MACLEOD stated that he was aware of the situation, and was considering how best to deal with it.

Mr. HASTINGS asked him to keep in mind that tuberculosis was infectious, and as many as 10 new cases had been traced to one individual. If the Minister really wanted to get rid of it he would have to deal with it by a certain amount of restriction and care of those who were spreading it. Mr. MACLEOD said that he had been anxious about this matter for some time. They were having a meeting soon with the Ministry of Housing and Local Government and the National Assistance Board to formulate a joint plan of action.

Development in Health Centres

Mr. A. BLENKINSOP (Newcastle-upon-Tyne, East, Lab.) asked if the Minister would make a statement on the development of health centres in view of the valuable experience gained at Harlow and elsewhere. Miss PAT HORNSBY-SMITH, the Parliamentary Secretary, stated that six new health centres had been provided under the National Health Service Act, 1946, in addition to 24 premises taken over as centres by local health authorities in 1948. A seventh new centre was opened formally the previous week, and a small number of schemes were at various stages of planning and construction. The Minister would continue to support, so far as he could, further experimentation where new facilities for local health authorities and general practice were needed and co-operation between these branches of the Service could be achieved. He welcomed the initiative of the Nuffield Provincial Hospitals Trust and other bodies in sponsoring other experiments at Harlow and elsewhere. These, together with the centres provided by local health authorities, would give valuable experience from which future projects would no doubt profit.

Mr. BLENKINSOP commented on the great value of the type of centre being developed at Harlow, and asked if the Minister would be prepared to consider whether any amendment of the Health Service Act might be necessary to encourage co-operation between the preventive and aftercare services. Miss HORNSBY-SMITH said the experience of these new centres and how they would work in a year or two after their inception would be of great value in judging their future use, but it would be idle to ignore the fact that the needs varied from area to area. While these centres might serve a vital need in a new community they were not always so applicable in old-established residential areas. They must work on the experience gained from the most useful schemes now under way.

London Doctors' Lists

Lieutenant-Colonel LIPTON (Brixton, Lab.) asked the Minister of Health whether he was aware that doctors' lists in the London area of the Health Service now contained 8,487 more names than the total population of the area; what the effect was on the cost of the Service; and what steps he was taking to rectify this anomaly. Miss HORNSBY-SMITH told him that the Minister knew of this estimate. Lieutenant-Colonel LIPTON said it was a fantastic situation, and apparently nothing had been done. What was the Ministry doing to ensure that these grossly inflated figures were not tolerated any longer than was absolutely necessary? Miss HORNSBY-SMITH replied that the executive councils and the doctors had been notified, but it was an extremely difficult matter, where no notification had been given, to check and trace immediately people who had died or who had moved from one area to another. The ultimate aim would be to have a central alphabetical index as well as the present numerical one. She wanted to correct a misapprehension that appeared in the question: this situation did not increase the payments to doctors, as they drew their fees from the general pool.

Hospital Amenity Funds

Mr. C. J. SIMMONS (Brierley Hill, Lab.) asked the Minister to what extent it was his policy to allow the use by hospital management committees of amenity funds for the carrying out of capital projects. Mr. MACLEOD answered that he welcomed proposals by hospital authorities for the use of non-Exchequer funds for urgently needed capital works and saw no reason to repay any such expenditure from the Exchequer. Mr. SIMMONS asked if the Minister would agree that adequate waiting-room accommodation, a dispensary, a pathological laboratory, occupational-therapy and staff-recreation rooms ought all to be part of the normal hospital services, and that it was unfair that the amenity fund should be used for these purposes to the detriment of the comfort of patients. Could he not agree to repay this money, if not immediately, at least when the economic situation looked a little better? Mr. MACLEOD said it would obviously be a bad system to repay expenditure of this nature, for all that would mean was that the wealthy hospitals—and there were many—could rebuild their premises completely if necessary and claim back all the money from the Exchequer. He must have regard to priorities.

Albomycin from Russia

Dr. STROSS asked the Minister of Health whether his attention had been drawn to the fact that many strains

of staphylococcal germs were resistant to penicillin but not to the antibiotic albomycin, discovered and developed in the U.S.S.R.; and whether he would approach the Ministry of Health in Russia for supplies of this antibiotic for clinical trial in British hospitals.* Mr. MACLEOD replied that members of the staff of the Medical Research Council discussed the properties of albomycin with the doctors who recently visited this country from the Soviet Union. The Council was endeavouring to obtain a supply of this antibiotic from the Soviet Union so that its properties could be investigated.

Letters to M.P.s

Mr. MACLEOD informed Dr. D. JOHNSON (Carlisle, Con.) that the persons or official bodies to whom an involuntary patient in a mental hospital was allowed to address unopened and unsupervised correspondence were set out in Section 41 (1) of the Lunacy Act, 1890. The detained person's Member of Parliament was not on the list, but it had always been the custom that letters to M.P.s should be forwarded. Dr. JOHNSON asked the Minister if he would make such an inclusion on the list. Mr. MACLEOD said he was not sure that it would be a suitable subject for legislation, but when the Royal Commission reported, perhaps in a few months' time, this was a matter that might well be considered.

Welfare Foods.—The Minister of Health is making inquiries into the consumption and distribution of welfare foods, and when they are complete he will consider whether any further action is required.

Hospital Building.—The total estimated value of hospital capital building projects now in progress, or to be started in the current financial year, including projects financed from non-Exchequer funds so far as information about these is available, is about £31.5m.

*Albomycin was the subject of a paper by Professor G. F. Gause in this *Journal*, November 12, p. 1177.

Vital Statistics

England and Wales in 1954

The birth rate in England and Wales during 1954 was 15.2 and the death rate was 11.3 per 1,000 population. The infant mortality was 25 per 1,000 related births and was the lowest on record. Deaths in the first week of life accounted for 60% of the infant mortality. The most notable falls in infant deaths during the past 30 years are those due to whooping-cough and bronchitis. The mortality from these diseases is now less than 5% of that in 1920; deaths from diarrhoea are less than 7%, and pneumonia deaths are now about 25% of the 1920 figure.

The death rate of children aged 1–4 was only 0.94 per 1,000 population; in 1920 it was 12.08. Mortality from infectious diseases in the pre-school child has fallen to a very low level. Deaths from all forms of tuberculosis were less than 4% of the 1920 figure, and only 2, 3, and 20 deaths were recorded from scarlet fever, diphtheria, and measles, respectively, compared with 590, 2,367, and 4,763 in 1920. Deaths from cancer in this age group (261) are treble the number of 30 years ago.

The death rate at ages 5–34 and 45–64 was the lowest ever recorded, and the death rate at ages 35–44 was 0.02 above the record low level of 1953. The death rates in each age group 65 and over were below the level of recent years but above the rates for earlier years.

Deaths from coronary heart disease continued to increase. The numbers were 41,688 for males and 23,983 for females; these were 3,435 and 1,701, respectively, above the numbers recorded in 1953. Deaths from cancer of the lung, bronchus, and trachea were 13,995 for males and 2,336 for females, increases of 1,114 and 85, respectively, on the totals for 1953. The number of suicides, 3,178 males and 1,865 females, were the largest since 1938, the increases on the 1953 totals being 158 males and 131 females. Deaths from accidents due to motor vehicles numbered 3,289 males and 1,158 females; they were 64 more for males and 137 more for females than in 1953. Falls at home or in residential institutions were responsible for 4,188 deaths, of which over 90% were of persons aged 65 and over. 28 male and 169 female deaths were of persons aged 100 or more.—*Registrar-General's Statistical Review of England and Wales for the Year 1954* (H.M.S.O., 12s. 6d.).

Index of Place Names

From the civil parish of Abbas and Templecombe in Somerset to the indefinable locality of Zouch in Nottinghamshire every place in England and Wales recorded in the 1951 census is listed alphabetically in two large volumes published this week (H.M.S.O., 3 guineas). Over 65,000 names are thus set out for the first time since 1924. To each place is assigned its administrative and electoral category and its population. Birmingham diocese tops the poll with a population of 1,461,547. Localities contending for bottom place include Seven Acres (Lincs), Burrow Island (Hants), and Staple Inn (London); these and several others returned a population of 0.

Infectious Diseases

A small rise occurred in the incidence of most infectious diseases during the week ending December 10 in England and Wales. The increases in the number of notifications included 99 for scarlet fever, from 1,127 to 1,226, 65 for whooping-cough, from 1,112 to 1,177, 65 for dysentery, from 615 to 680, 62 for measles, from 2,757 to 2,819, and 55 for acute pneumonia, from 462 to 517; the only large decrease was 263 for food-poisoning, from 451 to 188.

The largest rise in the notifications of scarlet fever was 29 in Yorkshire West Riding, from 173 to 202. The largest variations in the trends of whooping-cough were an increase of 36 in Yorkshire West Riding, from 121 to 157, and a decrease of 36 in Devonshire, from 48 to 12. The chief fluctuations in the returns of measles were rises of 41 in Lancashire, from 303 to 344, and 40 in Glamorganshire, from 285 to 325, and falls of 84 in Northamptonshire, from 235 to 151, and 35 in Pembrokeshire, from 76 to 41. 14 cases of diphtheria were notified, being 11 fewer than in the preceding week. Another 6 cases were notified from the outbreak in Staffordshire, Uttoxeter R.D.

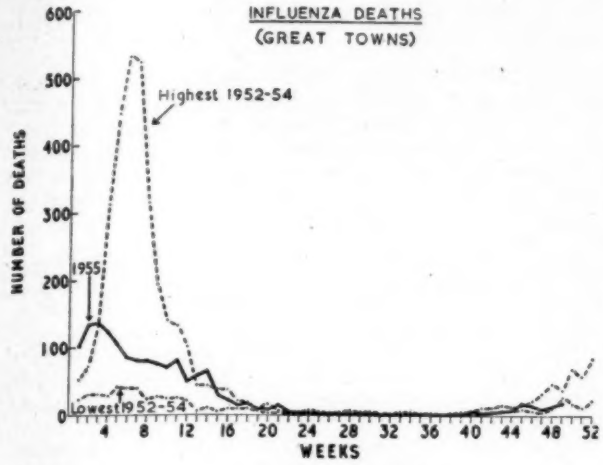
The number of notifications of acute poliomyelitis was 130; these were 14 more for paralytic and 1 more for non-paralytic cases than in the preceding week. The largest returns were London 23 (Greenwich 6, Woolwich 5, Islington 4, Lewisham 3), Yorkshire West Riding 12, Middlesex 11, Surrey 9, Warwickshire 8 (Birmingham C.B. 5), Lancashire 7, Devonshire 7 (Ottery St. Mary U.D. 4).

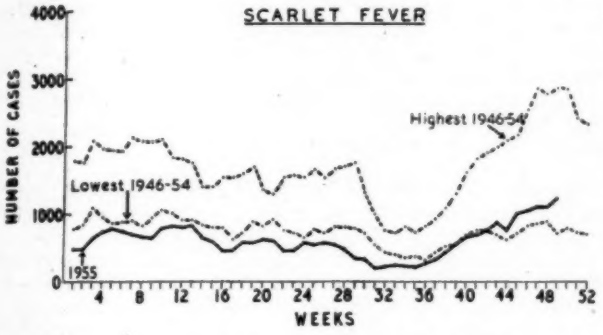
The chief centres of dysentery were Yorkshire West Riding 166 (Thorne R.D. 50, Huddersfield C.B. 38, Leeds C.B. 29, Bradford C.B. 10, Ilkley U.D. 10), Lancashire 145 (Liverpool C.B. 46, Droylsden U.D. 20, Stretford M.B. 13), London 49 (Islington 20), Surrey 45 (Carshalton U.D. 15, Leatherhead U.D. 12), Warwickshire 41 (Birmingham C.B. 28), Middlesex 32 (Ealing M.B. 10), Gloucestershire 24 (Bristol C.B. 23).

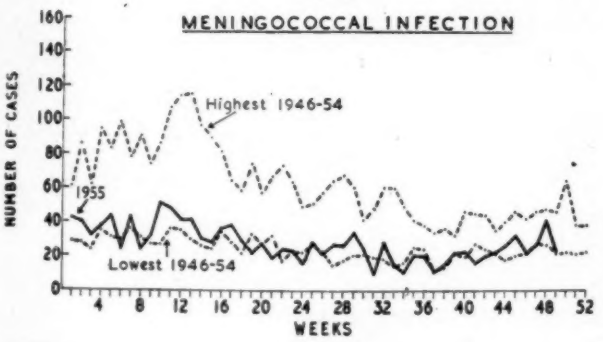
Graphs of Infectious Diseases

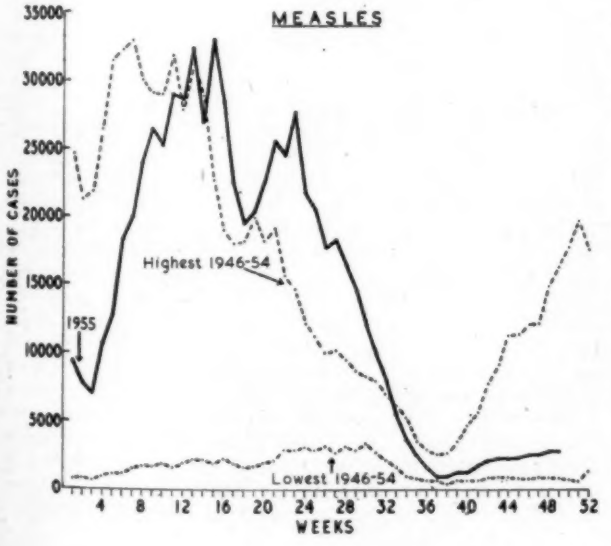
The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the nine

years 1946–54 (influenza, 1952–4) are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **December 10** (No. 49) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	14	0	16	0	4	15	0	8	0	
Dysentery	680	49	152	14	3	357	67	165	7	
Encephalitis, acute	4	2		0		1	0		0	
Enteric fever:										
Typhoid	1	0	1	0	2	2	2	4	0	
Paratyphoid	10	0	4 (B)	0		7	1	0	0	
Food-poisoning	188	22		1		134	11		0	
Infective enteritis or diarrhoea under 2 years				22	12				11	16
Measles*	2,819	20	65	10	47	6,298	473	493	312	61
Meningococcal infection	23	1	16	0	1	21	0	6	0	3
Ophthalmia neonatorum	27	2	6	1		30	6	3	0	
Pneumonia†	517	50	363	6		768	49	212	4	3
Poliomyelitis, acute:										
Paralytic	87	9	10	2	3	30	2	11	1	
Non-paralytic	43	14				13	2			
Puerperal fever§	221	39	11	4		214	33	6	1	
Scarlet fever	1,226	82	154	55	40	709	39	151	66	37
Tuberculosis:										
Respiratory	655	82	119	23		723	85	134	51	
Non-respiratory	83	6	11	1		85	13	22	11	
Whooping-cough	1,177	93	98	102	180	2,047	123	165	25	56

DEATHS in Great Towns	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	1	0	0	0	0
Dysentery	0	0		1		1	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	10	0	3	0		5	0	0	1	1
Influenza	19	0	0	1		56	5	1	0	0
Measles		0	0	0			0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	291	51	36	15	12	301	43	19	8	12
Poliomyelitis, acute	5	2			0	2	1			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	77	8	5	0	4	112	18	18	1	3
Non-respiratory		0	3	0	1		0	20	0	1
Whooping-cough	1	0	0	0	0	0	0	1	0	0
Deaths 0–1 year	238	26	40	14	13	226	32	23	6	12
Deaths (excluding stillbirths)	5,707	825	597	114	180	5,703	762	589	110	189
LIVE BIRTHS	7,138	1076	830	180	304	6,646	999	798	200	311
STILLBIRTHS	192	26	16			186	25	24		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

B.M.A. Library.—From January 1, the cost of outward postage on books borrowed by members from the B.M.A. Library will be borne by the Association, except in the case of borrowers in London postal areas adjacent to B.M.A. House. The relevant Library rule has been amended as follows:

Applications for books to be sent by post may be made in writing to the Librarian. The Association will meet all outgoing postal charges on parcels for destinations outside the area covered by the London postal districts N.1, N.W.1, W.C.1, W.C.2, E.C.1, E.C.4, and W.1, but the cost of returning books is to be borne by the borrower.

Regional Physics Department, Glasgow.—Hospital physics departments are nowadays extremely costly, both in equipment and in their need for highly specialized staff. To meet this situation the Scottish Western Regional Hospital Board has established a central physics department at premises in West Graham Street, Glasgow, formerly occupied by the out-patient dispensary of the Royal Hospital for Sick Children. The department is under the direction of Dr. J. M. A. LENIHAN, Ph.D., and it provides technical services of many kinds to hospitals and research teams in the board's area. The department's activities include teaching courses for the diploma in radiology; a workshop service for the design, construction, and repair of apparatus used in clinical research; dispensing of bulk supplies of radio-isotopes from Harwell and the Radiochemical Centre, and assistance in their use; production of short-lived radio-isotopes in a neutron tank for use in teaching and research; calibration of radiotherapy apparatus; measurements and calculations in connexion with radium and cobalt therapy; a monitoring service for *x*-ray workers; and collaboration in clinical research.

"Medicine."—Earlier this year the first issue of a new quarterly journal, *Medicine*, appeared from the Colombo Clinic, Ceylon. It will be devoted to the "advancement of medicine, surgery, and midwifery," but its special claim to attention is that it will be concerned primarily with the medical problems of the South-East Asian region. It is explained in an editorial that the regional organization of W.H.O. has drawn attention to this area's special needs, and the journal aims "to promote research into these urgent health problems, to provide facilities for publication of such research, and to offer an opportunity for discussion of such problems." The first issue, dated March, 1955, contains articles on the treatment of cardiac emergencies, fungi in the causation of disease in Ceylon, milk and human nutrition, the biochemistry of milk, and amoebiasis. The editors are Dr. A. NIMALASURIA and Dr. M. W. M. DE SILVA, and the opening issue includes a foreword by Dr. CHARLES NEWMAN, dean of the Postgraduate Medical School of London. The annual subscription is 16s. or 10 rupees. All communications should be addressed to the editors, the Colombo Clinic, 77, Dickman's Road, Colombo 5.

Emergency Bed Service.—At a meeting of the council of King Edward's Hospital Fund for London on December 13, with the DUKE OF GLOUCESTER presiding, Dr. G. F. ABERCROMBIE reviewed the work of the Emergency Bed Service since its inception in 1938. Ten years later, he said, the service was receiving 13,000 applications a year; this number was doubled immediately the National Health Service started; now the service expected to deal with 65,000 applications a year. The average time from the receipt of a general practitioner's request for a bed to the ordering of an ambulance was now 27 minutes. The bulk of cases were "general acute cases"; in summer 97% were admitted, but in winter, especially in times of epidemic, the admission rate tended to fall. The service had two methods for dealing with crises, continued Dr. Abercrombie: the individual patient for whom no bed could be found was referred by regional board machinery to the medical referee of the patient's hospital management committee for immediate admission; secondly, there was an elaborate warning system to hospitals which came into operation when admissions fell below 85%. Hospitals then took steps to provide more beds. As a result, since the influenza epidemic in 1953 the admission rate had not fallen below 80%.

King Edward's Hospital Fund for London.—The Fund has received a further instalment of £50,000 from the Nuffield Trust for the Special Areas. In founding this Trust Lord NUFFIELD provided that any sums that might accrue from repayment of loans or otherwise should pass to the Fund. A total sum of £1,650,000 has now been received by the King's Fund.

Cripples in Scotland.—Speaking at Stirling on December 10, Mr. J. NIXON BROWNE, Joint Parliamentary Under-Secretary of State for Scotland, expressed grave disquiet about the welfare of cripples in Scotland. "The hard fact is," he said, "in Scotland as a whole we don't even know how many crippled people there are. Here in Stirlingshire you have made a serious attempt to compile a register of handicapped persons, and as a result you have found out that in Stirling County there are over 300 crippled people for whom welfare services in one form or another could be provided. If the problem is the same in other areas it means that there are probably more than 15,000 crippled people scattered throughout the country, and many of these may be receiving no help from welfare services at all. Frankly, I feel that this is a blot on our record, and a challenge to us to get on and do something about it."

Medical Schools in the World.—Dr. J. L. TROUPIN, chief of W.H.O.'s Section of Assistance to Educational Institutions, has carried out a study of the number of medical schools in different parts of the world and their annual output in relation to the total population. His results (summarized in *Chron. Wld Hlth Org.*, 1955, **9**, 312) include the following:

Area	Medical Schools	Annual Output of Graduates	Total Population (Millions)
Africa	14	855	212
North America	122	8,930	234
South America	51	3,733	121
Eastern Asia	152	11,582	1,371
Western Asia	13	859	83
Europe	237	27,177	615
Oceania	6	753	14
Total	595	53,889	2,650

According to Dr. Troupin's figures only five countries included under the heading "Europe" have more than 10 medical schools—namely, U.S.S.R. (61), United Kingdom (27), France (24), Italy (21), and the Federal German Republic (18). Poland and Spain are stated each to have 10 medical schools. The full data are printed in *Bull. Wld Hlth Org.*, 1955, **13**, 345.

Permissible Exposure Levels in Atomic Plants.—Dr. G. HOYT WHIPPLE, of the University of Rochester Atomic Energy Project and a former Nobel Prize winner, is quoted in the *New York Times* as having called for a tenfold reduction of the maximum permissible exposure for workers in atomic power plants from the present 0.3 r per week to 0.03 r (see also last week's *Journal*, p. 1556). He was speaking at the Nuclear Engineering and Science Congress held earlier this month in Cleveland, U.S.A. Dr. Whipple is quoted as saying that a man receiving 0.3 r a week for 30 years might have his life expectancy reduced by three years, as judged by "extrapolation of the available life-span shortening data." He compared this with figures of 0.9 years from accidents of all kinds, and 1.8 years from cancer, for 30-year-old white males in the United States. If the permissible level were reduced to 0.03 r per week, Dr. Whipple estimated the reduction in life-span for a maximally exposed worker at four months—"a risk acceptable to most people."

Lead Glazes.—For some years now the pottery industry has been forbidden to use any but leadless or "low-solubility" glazes, because of the risk of lead poisoning. However, in some teaching establishments raw lead glazes or glazes containing a high percentage of soluble lead are still used. The Ministry of Education has now issued a memorandum to local education authorities and school governors (No. 517, dated November 9, 1955) with the object of restricting the use of raw lead glazes in such schools. The memorandum also includes a list of precautions to be observed when handling potentially dangerous glazes.

Awards for Research on Ageing.—Candidates wishing to enter for the 1955–6 Ciba Foundation Awards for research relevant to basic problems of ageing should submit their papers not later than February 10 to the Ciba Foundation, 41, Portland Place, London, W.1, whence further information may be obtained.

French Prize for Paper on Diabetes.—The French medical journal *Diabète* is offering a prize of 50,000 francs (about £50) for a paper on clinical, experimental, therapeutic, or medico-social aspects of diabetes. The paper must be written in French and submitted not later than January 31 to the editor, *Diabète*, 21, rue Saint-Fiacre, Paris 2, from whom further details may be obtained.

COMING EVENTS

Institute of Dermatology.—Semi-permanent exhibition on "Diseases of the Nails," January 3–24, 1956.

Marc Daniels Lecture.—Sir GEOFFREY TODD will deliver this lecture at the Royal College of Physicians, Pall Mall East, on January 12, 1956, at 5 p.m. He will speak on the chemotherapeutic control of fibro-nodular tuberculosis.

Second World Congress on Fertility and Sterility.—The International Fertility Association will hold its second world congress in Naples, May 18–26, 1956. Among the major topics for discussion are recent advances in the diagnosis and treatment of both male and female sterility. Further details and registration forms from Professor G. TESAURO, S. Andrea delle Dame, 19, Naples.

NEW ISSUES

British Journal of Pharmacology and Chemotherapy.—The new issue (Vol. 10, No. 4) is now available. The contents include:

METABOLISM AND EXCRETION OF ^{14}C-LABELLED DIETHYLCARBAMAZINE. D. R. Bangham.
THE MODE OF ACTION OF DIETHYLCARBAMAZINE INVESTIGATED WITH ^{14}C-LABELLED DRUG. D. R. Bangham.
THE EFFECT OF COMPOUND 48/80 ON MAMMALIAN SKELETAL MUSCLE. G. Sömjén and Ina E. Uyldert.
THE ACTION OF ANALGESICS AND NALORPHINE ON THE COUGH REFLEX. A. F. Green and Naomi B. Ward.
EFFECTS OF TRANSIENT CHANGES OF ACIDITY ON THE ISOLATED RAT'S UTERUS, WITH REFERENCE TO THE ASSAY OF OXYTOCIC ACTIVITY. P. Bentley and S. E. Dicker.
SIDE EFFECTS OF CHLORPROMAZINE HYDROCHLORIDE. E. M. Glaser and P. S. B. Newling.
THE AMOEBICIDAL ACTIVITY OF 2-DIETHANOLAMINO-5-NITROPYRIDINE. R. A. Neal and Patricia Vincent.
ALPHA-COCAINE. Roy Foster, H. R. Ing, and V. Varagic.
THE ENZYMIC HYDROLYSIS OF COCAINE AND ALPHA-COCAINE. H. Blaschko, Jean M. Himms, and B. C. R. Strömblad.
THE ACTION OF 5-HYDROXYTRYPTAMINE ON THE BLOOD VESSELS OF THE HUMAN HAND AND FOREARM. I. C. Roddie, J. T. Shepherd, and R. F. Whelan.
THE INHIBITION OF AMINE OXIDASE AND SPERMINE OXIDASE BY AMIDINES. H. Blaschko and Jean M. Himms.
THE ACTION OF ANTRYCIDE UPON TRYPANOSOMES IN VITRO. F. Hawking and June P. Thurston.
THE PARALYSING ACTION OF MORPHINE ON THE GUINEA-PIG ILEUM. W. Schaumann.
THE REACTIVATION BY OXIMES AND HYDROXAMIC ACIDS OF CHOLINESTERASE INHIBITED BY ORGANO-PHOSPHORUS COMPOUNDS. A. F. Childs, D. R. Davies, A. L. Green, and J. P. Rutland.
STIMULANT ACTIVITIES OF QUATERNARY AMMONIUM COMPOUNDS ON MAMMALIAN SKELETAL MUSCLE. G. L. Willcy.
THE USE OF SOME MOLLUSCAN HEARTS FOR THE ESTIMATION OF 5-HYDROXYTRYPTAMINE. J. H. Gaddum and M. K. Paasonen.
THE EXCRETION OF SALICYLATE. C. R. Macpherson, M. D. Milne, and Barbara M. Evans.
THE REVERSAL BY OXIMES OF NEUROMUSCULAR BLOCK PRODUCED BY ANTICHOLINESTERASES. R. Holmes and E. L. Robins.
INDEX TO VOLUME 10.

Issued quarterly; annual subscription £4 4s.; single copy 25s.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Ophthalmology.—The new issue (Vol. 19, No. 12) is now available. The contents include:

EXPERIENCE IN CLINICAL EXAMINATION OF CORNEAL SENSITIVITY. CORNEAL SENSITIVITY AND THE NASO-LACRIMAL REFLEX AFTER RETROBULBAR ANAESTHESIA. Jørn Boberg-Ans.
UVEITIS. A CLINICAL AND STATISTICAL SURVEY. George Bennett.
INVESTIGATION OF THE CARBONIC ANHYDRASE CONTENT OF THE CORNEA OF THE RABBIT. J. Gloster.
HYALURONIDASE IN OCULAR TISSUES. I. SENSITIVE BIOLOGICAL ASSAY FOR SMALL CONCENTRATIONS OF HYALURONIDASE. G. Mayer.
INCLUSION BODIES IN TRACHOMA. A. J. Dark.
TETRACYCLINE IN TRACHOMA. L. P. Agarwal and S. R. K. Malik.
APPLIANCES: SIMPLE PUPILLOMETER. A. Arnaud Reid.
LARGE CONCAVE MIRROR FOR INDIRECT OPHTHALMOSCOPY. H. Neame.

Issued monthly; annual subscription £4 4s.; single copy 8s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, January 2

DENTAL AND MEDICAL SOCIETY FOR THE STUDY OF HYPNOSIS.—At 11, Chandos Street, W., 8 p.m., Dr. A. A. Mason: Treatment of Oral Disorders by Hypnosis.

Tuesday, January 3

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. P. D. Samman: Tuberculosis Cutis.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Sir William P. MacArthur: Mediaeval Leprosy in the British Islands: What was It?

Wednesday, January 4

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. O. Oliver: Mycobacteria in Skin Diseases.

Thursday, January 5

FACULTY OF HOMOEOPATHY.—At Royal London Homoeopathic Hospital, 5 p.m., Dr. J. W. Fairbairn, Ph.D., Ph.C.: Plant Kingdom as a Source of Remedies.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Ophthalmology Lecture by Professor Arnold Sorsby: Some Dominantly Inherited Central Fundus Lesions.
ROYAL PHOTOGRAPHIC SOCIETY: MEDICAL GROUP, 16, Princes Gate, London, S.W.—7 p.m., Dr. C. Keith Simpson: Crime in Camera.

Friday, January 6

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. G. B. Dowling: Skin Tuberculosis and Sarcoidosis.
●MIDLAND CENTRE FOR NEUROSURGERY, Holly Lane, Smethwick.—8.15 p.m., Sir Charles Symonds: Particular Type of Migrainous Headache.
ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW.—At Royal Faculty of Physicians and Surgeons of Glasgow, 8.30 p.m., Professor G. MacG. Bull: Treatment of Disturbances in Body Water and Electrolytes.

APPOINTMENTS

ARDLEY, JOHN, M.B., B.S., D.P.H., Deputy Medical Officer of Health, and Deputy Principal School Medical Officer, County Borough of Coventry.

CORMAC, C. D., B.M., B.Ch., D.P.H., County Medical Officer of Health and Principal School Medical Officer, Lincolnshire (Lindsey).

CRAMOND, W. A., M.D., D.P.M., Physician-superintendent, Woodilee Mental Hospital, Lenzie, Glasgow.

CZYNIEWSKI, JOZEF, M.D., Junior Hospital Medical Officer in Anaesthetics to the West Cumberland Group of Hospitals.

DHANDA SATH PAUL, M.B., B.S., Surgical Registrar, Workington Infirmary.

GILLIATT, R. W., D.M., M.R.C.P., Assistant Consultant Physician for Diseases of the Nervous System, Middlesex Hospital, W.

LIVERPOOL REGIONAL HOSPITAL BOARD.—H. O. Williams, M.Ch.Orth., F.R.C.S., F.R.C.S.Ed., part-time Consultant Orthopaedic Surgeon to Whiston, Widnes Accident and Rainhill Hospitals; M. J. Garrett, M.B., B.Ch., D.M.R.T., Whole-time Assistant Radiotherapist to Liverpool Radium Institute.

PARKEN, DOUGLAS STUART, M.B., B.S., D.P.H., D.C.H., Deputy Medical Officer of Health, Borough and County of the Town of Poole, and Deputy Port Medical Officer.

RAYNER, MICHAEL JOHN, M.B., Ch.B., D.P.H., Deputy Medical Officer of Health and Deputy Principal School Medical Officer, County Borough of Wolverhampton.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Alms.—On November 23, 1955, at the Heswall Maternity Home, Cheshire, to Beryl, wife of Mr. M. Alms, M.Ch.Orth., F.R.C.S., a daughter—Georgina.

Coles.—On December 12, 1955, to Elizabeth (formerly Morris), wife of Surgeon Lieutenant Ross Coles, R.N., of 7, Selsey Avenue, Southsea, a son—Robert Jonathan.

DEATHS

Booth.—On November 27, 1955, at Newbury District Hospital, Mary Irene Booth (formerly Symons), M.R.C.S., L.R.C.P., of Tydehams, Newbury, Berks, aged 62.

Hall.—On November 30, 1955, Samuel Hall, M.B., B.Ch., of Clifton Lodge, St. Margaret's Drive, Twickenham, Middlesex, late of Golcar, near Huddersfield, Yorks, aged 59.

Henderson.—On November 26, 1955, at the home of his daughter, 94, St. James's Avenue, Beckenham, Kent, George Henderson, L.R.C.P.&S.Ed., L.R.F.P.S., Lieutenant-Colonel, I.M.S., retired, late of India and Australia, aged 76.

Leeper.—On November 29, 1955, Bertram Charles Alexander Leeper, L.R.C.P.&S.I., of 9, Mountjoy Road, Huddersfield, Yorks.

Price.—On November 28, 1955, at St. Mary's Hospital, London, W., Alan Vandyke Price, M.B., M.R.C.P., aged 31.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Combined Use of Penicillin and Sulphonamides

Q.—*A combination of sulphonamides and penicillin has been recommended for the treatment of puerperal sepsis. Surely penicillin acts best on bacteria in a state of activity, and therefore should not be given at the same time as sulphonamides, which tend to be bacteriostatic.*

A.—The type of antagonism referred to has been demonstrated only between certain pairs of antibiotics, one of which is bactericidal—for example, penicillin—and the other bacteriostatic. Although the sulphonamides are also bacteriostatic, there is no antagonism between them and penicillin: on the contrary, many observations on the therapy of experimental animal infections have shown their combined action to be synergic, and clinical experience has been held to confirm this. The explanation of this apparent paradox is not entirely clear, but a reasonable hypothesis is offered by Klein and Kalter,[1] who are among many authors to have observed similar synergic action *in vitro*.

It has also to be remembered that sulphonamides and penicillin have different ranges of activity: some bacteria are much more susceptible to one than the other, and the combination therefore offers protection against a greater variety of infections. For example, Prince[2] reported excellent results from this combination in the prevention of urinary infection in connexion with prostatectomy: here penicillin doubtless suppressed streptococci and staphylococci and the sulphonamide dealt with coliform bacilli. Post-partum uterine infection can also be caused by any of a variety of bacteria, and a combination affording broad "cover" is therefore justified for its initial treatment.

REFERENCES

1 Klein, M., and Kalter, S. S., *J. Bact.*, 1946, **51**, 95.
2 Prince, C. L., *J. Urol.*, 1946, **56**, 121.

Stridor after Extubation

Q.—*What is the cause and treatment of the post-operative stridor and dyspnoea which occasionally occur just after a patient has been extubated?*

A.—An intratracheal tube is a gross foreign body, and as such excites powerful laryngeal and tracheal protective reflexes. It must be rare that in these circumstances no traumatization of the larynx or tracheal mucous membrane occurs. When a tube has been in place for perhaps over an hour, prolonged pressure on one or more spots in the trachea and larynx is likely. When the tube is finally removed the scraping of the tube on the larynx is added to the other traumata. Laryngeal and respiratory reflexes, of which stridor and dyspnoea are but two symptoms, are inevitably brought into action. Other effects may also be produced—mucus and salivary secretion, and inhibition of respiration sometimes for long enough to produce marked cyanosis. All these effects not uncommonly follow extubation in lightly anaesthetized patients. Anaesthetists should therefore avoid handing the patient over to the care of a nurse or orderly at this point, but should wait until respiration is once again normal and unimpaired. No treatment is required in the majority of cases, the stridor and dyspnoea disappearing in a few minutes. In others, the administration of oxygen, perhaps with gentle assistance, will prevent cyanosis during the few minutes in which normal respiration is being established. Should the stridor and dyspnoea persist, there is a strong suspicion either that some stomach contents which were in the pharynx have reached the larynx or that some injury, although perhaps quite small, has occurred to the larynx. Careful endoscopic examination of these parts is then indicated.

Position of the Head after Head Injury

Q.—*What is the correct position for the head and shoulders in the first-aid treatment of cases of unconsciousness due to head injury? One first-aid book states that the head and shoulders should be raised in all cases, another varies this according to the colour of the face, while orthodox hospital practice appears to be to keep the head low in all cases.*

A.—The questioner's difficulty is a real one and arises from the need in a handbook of first-aid to provide rules for the guidance of non-medical workers, although it is clear that no rule will invariably prove a safe guide. The advantages of elevation of the head and shoulders are that it relieves intracranial venous congestion and increases the respiratory exchange. If, however, the airway is obstructed by blood or secretions, the disadvantages of this position would greatly outweigh its advantages and the patient would be better nursed with the head and shoulders lowered. The advantages of the lowered position of the head and shoulders are that, where the patient is in the lateral position, obstruction of the airway by backward displacement of the tongue is prevented, and blood and secretions drain from the mouth and do not accumulate in the pharynx. Further, should the patient vomit, the risk of aspiration of vomitus is greatly reduced. Shock may likewise be benefited.

Thus, after admission to hospital, in the early stages the patient should be nursed on his side with the head lowered. Later, when the air passages can be kept clear by means of suction, elevation of the head and shoulders is beneficial. However, the individual who has sustained a severe head injury may also have sustained a spinal fracture, and as a *first-aid* measure the lateral position would be dangerous. The patient must therefore be nursed on his back. If there is no evidence of respiratory obstruction the head should be raised; if there is shock, or if secretions accumulate in the pharynx, lowering of the head would be the right procedure.

Ribonuclease and Cell Metabolism

Q.—*In your report of the Third International Congress of Biochemistry (September 3, p. 614) there is a reference to the effects of ribonuclease on tumour cells. Would ribonuclease be worth trying in a patient with inoperable carcinoma?*

A.—The effects on living cells of ribonuclease, a nucleolytic enzyme, produced from beef pancreas according to Kunitz[1] and purified according to Hirs, Moore, and Stein,[2] have been studied experimentally with different material: amphibian eggs (Ledoux *et al.*[3]), amoebae (Brachet[4]), *Bacillus megatherium* (Groth[5]), influenza virus (Le Clerc[6]), ascites tumours (Ledoux[7]), and solid tumours (Ledoux[8]). In most cases interference with protein and nucleic acid metabolism and with growth or cell division has been observed. Although very interesting from an experimental point of view, it appears that much more research is necessary to assess fully the results with this enzyme, particularly on abnormal cells. So far as is known, no systematic trials in human beings suffering from various forms of malignancy have been carried out yet, probably because the long-term effects (anti-tumour, immunological, toxic) have not been explored sufficiently to warrant such an undertaking at the present moment.

REFERENCES

1 Kunitz, M., *J. gen. Physiol.*, 1940, **24**, 15.
2 Hirs, C. H. W., Moore, S., and Stein, W. H., *J. biol. Chem.*, 1953, **200**, 493.
3 Ledoux, L., Le Clerc, J., and Vanderhaeghe, F., *Nature (Lond.)*, 1954, **174**, 793.
4 Brachet, J., ibid., 1955, **175**, 851.
5 Groth, D. P., Résumés des Communications, 3ème Congrès International de Biochimie, 1955 (No. 8-21).
6 Le Clerc, J., ibid. (No. 8-38).
7 Ledoux, L., *Nature (Lond.)*, 1955, **175**, 258.
8 Ledoux, L., ibid., 1955, **176**, 36.

Dietary Potassium in Acute Nephritis

Q.—*Is it helpful to reduce the dietary intake of potassium in the treatment of acute nephritis? If so, what foods should be banned?*

A.—There is no advantage in reducing the dietary intake of potassium in acute nephritis unless the patient develops anuria or prolonged oliguria. Under these circumstances there will be retention of nitrogenous waste-products in addition to failure to excrete electrolytes, and the patient is then best treated by giving the Bull–Borst fat-carbohydrate (protein and electrolyte-free) diet by intragastric drip.

Colouring Atropine Eye-drops

Q.—*What would be the best material for colouring atropine sulphate eye-drops blue, so as to prevent their misuse?*

A.—Methylene blue should be quite suitable for colouring atropine sulphate eye-drops. It has been used as an antiseptic for the eyes in the form of drops, containing from 1 to 2%, so that it is unlikely to cause any unpleasant local effects in the much smaller concentrations needed for colouring purposes.

There are no reports of any incompatibility between atropine sulphate and methylene blue, and this is unlikely on theoretical grounds. The addition of a concentration of 1 in 100,000 of methylene blue to eye-drops containing 1% of atropine sulphate gave a deep sky-blue colour with no signs of any precipitate or other evidence of incompatibility. The solution remained clear on standing for 24 hours. This concentration, therefore, or even a smaller one, of methylene blue should be suitable for colouring the eye-drops.

Immunization of the Pre-school Child

Q.—*What course of immunization is recommended for (a) a child of 4½ years who has had no previous immunization except B.C.G.; (b) a child of 2 years who has not been previously immunized? Both have been successfully vaccinated against smallpox.*

A.—Both children may be given three doses of diphtheria–tetanus–pertussis (triple) prophylactic at intervals of four to six weeks as a primary course. Triple is preferred to diphtheria–pertussis prophylactic, as it ensures active protection against tetanus without additional inconvenience to either doctor or patient. With regard to boosting, the child aged 4½ years might receive one injection of diphtheria–tetanus prophylactic at about the middle of school life. The child of 2 years could be given this combined prophylactic before school entry and also towards the end of school life. It may be noted that the triple prophylactic is not being advised for boosting in either case: the reason is that the pertussis constituent is of less importance for children of school age, in whom whooping-cough tends to be less severe.

Additional boosting doses of the separate antigen may be needed on exposure to diphtheria or whooping-cough (in the case of the younger child) or after dirty cuts. In the event of injury, tetanus toxoid is being used increasingly instead of antitoxin for actively immunized persons. However, tetanus antitoxin should always be given after injury (*a*) if there is any doubt whether a patient has received a full primary course, plus adequate boosting doses, of tetanus toxoid, and (*b*) if the wounds are multiple or prophylactic treatment has been unduly delayed.

Sensory Changes due to a Prolapsed Disk

Q.—*What is the mechanism of the sensory changes in cases of prolapsed intervertebral disk?*

A.—The common intervertebral disk protrusions occurring in the lumbar and cervical portions of the spinal canal are laterally placed. Here their neurological effects are produced by stretching and compressing a single spinal nerve (one anterior or one posterior root surrounded by a dural sheath) in its course from the theca to an intervertebral foramen. Sensory changes are the result of this trauma to one posterior root and are therefore restricted to the dermatome to which it is distributed. Because of the overlap in the distribution of spinal roots the changes are limited to a part of the dermatome only and are revealed by a reduction rather than a loss of cutaneous sensibility in this area.

The much less common central protrusions compressing either the spinal cord or all the roots of the cauda equina may give rise to a sensory reduction or anaesthesia to a segmental level corresponding to the site of the cord compression, or in the dermatomes supplied by the involved roots of the cauda equina. This picture is similar to that occasioned by other lesions causing compression in the spinal canal.

Management of an Old Femoral Thrombosis

Q.—*What treatment is advised for swelling of a leg due to an old puerperal femoral thrombosis? The leg looks nearly normal in the morning, but increases in size during the daytime; the swelling is particularly noticeable at the patient's periods.*

A.—It is assumed that the fact that the swelling is due to femoral vein thrombosis has been established, and that it is not due to some other cause such as lymphatic disease.

The treatment is conservative, unless there are any large incompetent superficial varices which require surgical treatment. The patient should sleep with the foot of the bed elevated 6 in. (15 cm.). A well-fitting elastic stocking must be worn during the daytime. This should fit snugly when first applied in the morning. It should extend from the bases of the toes to just below the knee. The plastic net type of stocking sacrifices support for appearance and is useless. In severe cases a heavy elastic bandage is necessary. The patient should avoid unnecessary standing and elevate the leg whenever possible on sitting down.

None of this treatment is likely to be popular with the patient, but she must be warned that neglect of the limb may result in eczema, ulceration, or other complications.

Drugs to Stimulate Lactation

Q.—*Is there an effective drug for stimulating the secretion of milk in lactating mothers?*

A.—No. Both Lugol's iodine, 5 minims (0.3 ml.) three times a day, and thyroid, 1–2 gr. (65–130 mg.) three times a day, have been recommended, but the results are inconsistent. Similarly preparations stated to contain pituitary lactogenic hormone have proved disappointing in clinical practice.

Effect of Exogenous Thyroid on Endogenous Production of Thyroid Hormone

Q.—*A patient with migraine has benefited from a course of thyroid, 1 gr. (65 mg.), twice a day. The right lobe of the thyroid gland has now enlarged. Will continuation of thyroid medication result in the gland ceasing to function?*

A.—In a normal person the production of thyroid hormone is dependent on the secretion of the thyroid-stimulating hormone of the anterior pituitary gland, thyrotrophin. If the blood level of thyroid hormone is raised, the secretion of thyrotrophin is reduced and there results a diminished secretion of thyroid hormone by the thyroid gland. If we take it that the normal thyroid gland secretes in 24 hours the amount of thyroid hormone contained in 5 gr. (325 mg.) of thyroideum siccum, then the administration of 2 gr. (130 mg.) of thyroideum siccum per day will depress the secretion of thyrotrophin to a degree that will result in the thyroid secreting the equivalent of only 3 gr. (195 mg.) of thyroideum siccum. It will thus be seen that the activity of the thyroid gland is reduced, but that the amount of thyroid hormone in the blood stream is the same as it was before the 2 gr. (130 mg.) of thyroideum siccum was administered. Hence the administration of 2 gr. of thyroideum siccum can have no effect on any bodily function

apart from its depressant action on the thyroid gland. The administration of 5 gr. (325 mg.) of thyroideum siccum per day would cause the thyroid to cease to function, so that the blood level of thyroid hormone could remain unchanged.

European Children and Malaria

Q.—*How serious nowadays is the risk to a young European child of a sojourn in a hyperendemic malarial area?*

A.—There is always some risk to a young European child in an area in which malaria is endemic, but it is small if adequate precautions are taken. Antimalarial measures must include both the administration of drugs and protection against mosquito bites.

Drugs recommended for children are the 4-amino-quinolines (chloroquine, amodiaquine), proguanil, and pyrimethamine. Doses, which can be found in the relevant textbooks, must be given regularly. In areas where there is evidence of the existence of proguanil-resistant strains of parasite, proguanil and pyrimethamine should not be given. Otherwise the three drugs are about equally effective. After leaving the endemic area and stopping the antimalarial drug, relapse may occur in benign tertian, quartan, and ovale infections. Malignant tertian infections are usually eradicated by suppressive therapy and should therefore not relapse.

Personal protective measures are every bit as important as suppressive therapy. They are largely dependent on parental control and must be rigidly enforced. The child should be in bed before sundown and should sleep and rest under netting or in quarters properly screened with wire of suitable mesh. The major source of infection to mosquitoes and consequently to man is the young native child, who should not be permitted to live on or near the premises. Exposure in dangerous areas should be avoided by insistence on reasonable clothing, early bed-time, etc. In most large centres local antimalarial control will probably have lowered the immediate risk of infection, but special care will be needed when travelling or visiting other less protected areas. Any slackening of precautions will lead to disaster. All too often failure is blamed on the antimalarial drug when the parents are really at fault.

Systemic Lupus Erythematosus

Q.—*What is the modern treatment and prognosis for lupus erythematosus disseminatus?*

A.—Systemic lupus erythematosus, to which the questioner probably refers, is a disease of unknown aetiology. Only on the rare occasions when this particular morbid process is thought to have been provoked by some specific infective or toxic cause can specific treatment be instituted. Otherwise treatment is empirical and symptomatic, and the prognosis bad.

Rest plays an important part in the early stages of the disease, and in the majority of patients corticotrophin and cortisone suppress symptoms without apparently affecting the underlying disease. However, the suppression of disturbances of function that would otherwise prove fatal may upon occasion increase the chances of a spontaneous recovery. The grave cardiac and renal manifestations of the disease are among the more important in determining the prognosis.

Danger of Cement Dust to Man and Farm Animals

Q.—*Is cement dust from the chimney of a cement works harmful to those who breathe it, or to animals fed on pastures or hay coated with the dust?*

A.—Cement dust is inhaled in high concentrations by cement workers, and so far has never been shown to produce any radiological changes or any other injury to the lungs, except when it contains an unusually high proportion of silica. The ingestion of deposited dust by animals seems unlikely to be harmful; if it were, one would expect to hear complaints very quickly.

NOTES AND COMMENTS

Viscous Semen.—Dr. C. E. M. WARE (Taunton) writes: With regard to your expert's answer to the problem about viscid semen ("Any Questions?" November 26, p. 1343) I have had 133 such cases during the past eight years. I regard it as a testosterone deficiency and thus accessory gland dysfunction. In all these cases sperm motility is not sustained. I give methyltestosterone by mouth, commencing with a very small dose in order to obviate any depression of spermatogenesis. I start with 25 mg. *a week* and have specimens at monthly intervals, increasing the dose as necessary until one gets a specimen that liquefies completely, and motility is sustained. I know of 24 pregnancies within six months of adequate therapy—the couples having previously been trying for children for periods of not less than two years. I have one case in which three pregnancies have occurred following therapy—although on the second and third occasions the couple tried for children for at least six months before seeking further treatment. I am now in the process of doing a follow-up on these cases and therefore do not know of all the pregnancies that may have followed treatment, but I do feel that these figures are of significance, and therefore I disagree with your expert that viscid semen has no bearing on infertility and also that no treatment is known which will alter this seminal characteristic. All my cases that have persisted with treatment have eventually produced a specimen that liquefied completely.

OUR EXPERT replies: I am very interested to hear of Dr. Ware's findings, but I remain rather sceptical. There is no question that men known to have androgenic deficiency, but still able to ejaculate, do not ordinarily produce viscid semen; on the contrary, their semen is usually quite watery in consistency. I cannot therefore agree that viscid semen is evidence of androgenic deficiency, and I have not myself seen any constant effects from testosterone therapy in such individuals. As I pointed out in my original reply, a normal post-coital test may be found in some cases even when the semen is viscid, and in such circumstances I cannot believe that viscidness, *per se*, contributes to infertility. I have also had experience of several pregnancies occurring where the husband's semen has been viscid but no therapy had been given to him.

Hiccup During Anaesthesia.—Dr. JEAN CARSTAIRS (Jamaica) writes: The correspondence in "Any Questions?" on this subject (August 13, p. 447; October 1, p. 862) makes it clear that the method of stopping hiccups during anaesthesia first described by Dr. Ram Murthi is not generally known. A soft rubber catheter is lubricated and passed down the nose until the tip reaches the larynx. It is there briefly agitated and then withdrawn. This manœuvre nearly always stops the hiccups, does not cause laryngeal spasm, and avoids undesirable alterations both of the depth of anaesthesia and of the carbon-dioxide concentration of the blood. Presumably the insult to the vagus interrupts the hiccup reflex. This method would not be suitable for the conscious patient. The most accessible part of the vagus is the branch which supplies the posterior half of the tympanic membrane (once called "the alderman's nerve"). An injection of ice-cold water into the external auditory meatus might be effective in stopping hiccups in the conscious patient. I have long wished to try this, but have never managed to have some ice, an aural syringe, and a chronic hiccupping patient together at the same time.

Correction.—In the Table of Infectious Diseases and Vital Statistics for the week ending November 19 (*Journal*, December 10, p. 1458) the cases of acute poliomyelitis notified should have been recorded as follows: England and Wales, paralytic 111, non-paralytic 63; London, paralytic 11, non-paralytic 9.

Books of "Any Questions?"—The second and third volumes of "Any Questions?" are available, price each 7s. 6d. (postage 6d.), from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or through any bookseller. Each contains some 200 selected expert answers, and the third volume a cumulative index to the three published books.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.
ADVERTISEMENTS should be addressed to the Advertisement Director, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: *Britmedads, Westcent, London.*
MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association. TELEPHONE: EUSTON 4499. TELEGRAMS: *Medisten, Westcent, London.*
B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.